DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMITTEE ON BLOOD SAFETY AND AVAILABILITY

Twenty-First Meeting

Volume I

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Hyatt Regency Capitol Hill Hotel
Capitol Room
400 New Jersey Avenue
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P A R T I C I P A N T S

Mark Brecher, M.D., Chairman

Larry Allen
Judy Angelbeck
Celso Bianco, M.D.
Ronald Gilcher, M.D.
Paul F. Haas, Ph.D.
William A. Heaton, M.D.
Christopher Healey, J.D.
W. Keith Hoots, M.D.
Jeanne Linden, M.D.
Karen Shoos Lipton, J.D.
Lola Lopes, Ph.D.
Gargi Pahuja
John Penner, M.D.
S. Gerald Sandler, M.D.
Mark Skinner, J.D.

Non-voting Government Representatives

James S. Bowman III, M.D.
Jay Epstein M.D.
Mathew Kuhnert, M.D.
Harvey Klein, M.D.
Captain Lawrence McMurtry
LTC Ruth Sylvester

C O N T E N T S

P R O C E E D I N G S

DR. BRECHER: I'd like to welcome everybody to the 21st meeting of the Advisory Committee on Blood Safety and Availability. This meeting will center on the role of liquid and frozen blood reserves as a strategy to preserve the blood supply in the face of reductions in supply and increases in demand.

I'm going to turn the meeting over to Mac McMurtry, who will introduce new members and read our conflict of interest statement.

CAPTAIN McMURTRY: In fact, we do have new members with us today that I'd like to introduce. If I do it alphabetically, I think I can keep everybody's name in mind.

Judy Angelbeck is with us today from Pall Corporation; Andrew Heaton, Chiron; Chris Healey with PPTA. Dr. Jerry Sandler is here from Georgetown Hospital, right? Did I do that right?

We have two new ex officio members. Once again alphabetically, we have Mathew Kuhnert from CDC and Lieutenant Colonel Ruth Sylvester from the

DOD Blood Program. She's wearing blue so she must be from the Air Force as well.

Let me call the roll so that we have that done officially, and then I'll get to read to you again this delightful conflict of interest statement that you all enjoy so much.

Mark Brecher, here; Larry Allen; Judy Angelbeck. Celso is not here. Ron Gilcher. Dr. Gomperts is not going to be able to be with us today. Dr. Heaton is here. I just called his name. Chris Healey, here. Paul Haas, here. Dr. Hoots will be with us later on today. He's having some flight issues. Dr. Linden; Karen Lipton; Dr. Lopes; Ms. Pahuja. John Penner is not with us today. Dr. Sandler; Mr. Skinner. And Mr. Walsh is not with us today. He's otherwise occupied.

Let's do the conflict of interest and ethics thing. Everybody sit back, get comfortable.

Ethics rules for Committee members appointed to the Federal Advisory Committee are appointed to special advisory committees as special government employees. The Ethics Division of the

Office of General Counsel has asked that I explain the rules that apply to you as special government employees, or SGEs. If you have any questions, let me know. I'll seek assistance from the attorneys at the OGC, the Office of General Counsel, and get the questions answered for you.

All matters I'll be discussing are explained in more detail in the handout that I will provide to you but haven't as yet.

Pursuant to several sections of the U.S. Public Health Service Act as amended by the U.S. Code and various provisions of the Federal Food, Drug, and Cosmetic Act, the Secretary of the United States Department of Health and Human Services has authority to carry out research in health fields, including diseases involving blood and blood products and for issuing and enforcing regulations concerning the collection, preparation, and distribution of blood and blood products.

The Advisory Committee for Blood Safety and Availability will advise, assist, consult with, and make recommendations to the Secretary and the

Assistant Secretary of Health regarding these broad responsibilities. The Chair and other members are special government employees appointed to perform duties on an intermittent basis not to exceed 130 days during any 365-day period. I have U.S. Code reference for this authority if anybody would like to see it.

All Committee members appointed as SGEs are required under the Ethics in Government Act, amended by the Ethics Reform Act of 1989, to file a financial disclosure report form annually. You'll be getting one of those in the mail soon.

The information reported is used to determine the matters for which a Committee member must be disqualified under the criminal conflict of interest statutes. Let me discuss that criminal ethics statute for just a second.

SGEs are subject to a number of criminal ethics statutes. Violation of the bribery provision imposes substantial fines and/or imprisonment. A violation of any other U.S. Code provision is punishable as a Class A misdemeanor

and subject to a fine and imprisonment. Willful violation of the code elevates the commission to a felony, and the Attorney General may opt for several penalties. In a civil action, the government need only prove the violation by a preponderance of the evidence rather than the criminal standard requiring proof beyond reasonable doubt. I need to describe these various statutes.

First is a bribery statute which prohibits Federal employees, including SGEs, from seeking, accepting, or agreeing to receive anything of value in return for being influenced in the performance of an official act. There is an example of a person receiving a brown paper bag of money in exchange for a recommendation to the Secretary.

There is the anti-representation statute which prohibits an SGE from receiving compensation for representational services rendered by an employee or another person before the HHS or any other Federal agency or other specified entity, such as a court or committee, in any particular matter involving a specific person, one, in which

the SGE has participated personally and substantially as a government employee or, two, which is pending in a government agency in which the SGE is serving if the SGE has served more than 60 days during the immediately preceding 365 days.

The post-employment statute imposes a lifetime ban on a former SGE from representing any person or entity to the HHS or other Federal agency or other specified entity, such as a court, in any particular matter involving a specific party in which the former SGE participated personally and substantially while serving in the government.

The financial conflict of interest statute, the main conflict of interest statute, prohibits an SGE from participating personally and substantially in any particular matter that could affect the financial interest of the SGE, the SGE's spouse, minor children, general partner, and organization in which the SGE serves as an officer, director, trustee, general partner, or employee, or an organization with which the SGE is negotiating or with which the SGE has an arrangement for

prospective employment.

Specifically, you as an SGE cannot work on matters affecting your financial interest or those of your spouse, minor children, or organization with which you are affiliated. An example would be owning a stock in Pharmaceutical Company X which produces a test for, in this case, viral contamination. You cannot participate in decisions or discussions to partner with Company X to promote that test.

You must also disqualify yourself from matters affecting your financial interest as a class. For example, using the same scenario of Pharmaceutical Company X, you own stock in this pharmaceutical company that produces a test for viral contamination. You cannot participate in decisions regarding testing for viral contamination. However, broad matters of national policy that don't focus on a specific industry are not a problem.

Under regulatory waiver issued by the Office of General Ethics, you may participate in

matters affecting your employees as a matter of class but not any matter that will affect the employees specifically. For example, you may recommend a grant program be established even though the university for which you work will be eligible, but you may not participate in the consideration of a specific grant application submitted by your university.

Additionally, while this exemption will allow you to participate in any matter of general applicability, it would affect the financial interest of that--I beg your pardon, it would affect the financial interest of a specific university, we'll say Harvard Medical School and/or Harvard University, as a member of a discrete and identifiable class of similarly situated medical schools or universities. The exemption will not protect you from violation of the criminal statute if the matter will have a special or distinct effect on Harvard Medical School or Harvard University. This means that you can participate in generally applicable matters such as legislation,

regulation, or policy that affects medical schools or universities as a class. The same rule applies with respect to other types of employees so that if you work for a pharmaceutical company, you can participate in matters affecting your employer as a member of a class. However, if you have any other interest besides employment, such as stockholding, you must disqualify from all matters even if it only affects that employer as a part of the industry sector.

On the other hand, another regulatory exemption if you're under regulatory--if you're under another regulatory exemption, if your financial interest is in publicly traded securities valued at less than $25,000, you can work on matters affecting as a part of the industry sector. But, again, you have to avoid matters that will have specific effect on that company. You may receive compensation for speaking engagements or writing undertaken in a personal capacity. However, you may not receive compensation for speaking or writing that was undertaken as part of

your official duties as a member of the Committee that draws on non-public information to which you have access as a member of the Committee, nor if the invitation was extended primarily because of your membership on the Committee.

You may receive gifts where circumstances make it clear that the gift was not offered as a result of your membership on the Committee. Generally, you should not use your position to imply that the Committee or government endorses your private activities. You should not disclose non-public information to which you have access. You may state your personal opinions, but you should not imply that you are speaking for the Committee unless you are actually authorized to do so.

There is an issue regarding fundraising. You may do personal charitable fundraising, but you may not personally solicit funds from anybody who has business before the Committee. Under the Constitution, while you serve as an SGE, you may not have an employment relationship with the

Federal Government--with a foreign government; that is, you can't be reimbursed by a foreign government. This may include foreign public universities and government-owned companies, depending on the degree of control of the Federal Government--beg your pardon, the degree of control the foreign government exercises. Under the Foreign Gifts and Declarations Act, you generally may not accept gifts from a foreign government unless the worth is under $260.

In your official capacity or as a group, Committee members are prohibited from engaging in any activity which directly or indirectly encourages or directs any person or organization to lobby one or more Members of Congress. When authorized, Committee members may appear before any individual or group for the purpose of informing or education of the public about a particular policy or legislative proposal. The Committee members may also communicate to Members of Congress at the request of any Representative or Senator. Communications to Members of Congress initiated by

Committee members in their official capacity as members of the Committee should be coordinated through the Office of the Assistant Secretary for Legislation.

As private citizens, Committee members may express their personal views, but not the view of the Committee as a whole or the opinions of HHS to anyone. In so doing, Committee members may state their affiliation with the Committee, may factually state the Committee's official position on a matter to the extent that non-public information is not used, but may not take new positions or represent those views as the Committee's position on the matter.

Moreover, in expressing their private views, as with all other personal non-government activities, Committee members are not permitted to use U.S. Government computers, copiers, telephones, letterhead, staff resources, or other appropriated funds. All personal activities must occur off-duty time.

And, finally, the Hatch Act prescribes

that restrictions on certain political--the Hatch Act does prescribe certain restrictions on certain political activities by Federal employees. Unlike the criminal statutes and most other ethic rules which are fully applicable to an SGE throughout your entire term of appointment, the Hatch Act restrictions apply only during the period of the day in which you are actually performing government duties. For example, if an SGE attends an Advisory Committee meeting from 8:00 to 1:00 and at 3 o'clock you should attend some other type of political meeting, you may do that so long as, as I said, it occurs after work hours on your time.

And that's that. Let me add before I leave that we now have Dr. Bianco with us and Dr. Epstein with us.

Thank you.

DR. BRECHER: Any questions on the conflict of interest?

CAPTAIN McMURTRY: Everyone sits in stunned silence.

DR. BRECHER: I just want to remind

members of the Committee that when they do have a comment to make, be sure to turn the microphones on because there are transcripts being made of the meeting. If there are no questions, we'll move on to a review of the Committee recommendations regarding reserves, and I will be summarizing those.

Over the course of the last few years, this Committee has visited the issue of availability of blood products, specifically red cells, on several sessions. And so I have gone back through the Committee resolutions and tried to summarize the most pertinent resolutions that have been made.

This goes back to April 2001. Many Committee members will remember--this was before I was on the Committee--where the Committee stated that whereas patient access to a safe and available blood supply is a public health priority, the Advisory Committee recommended that the Secretary of Health and Human Services and the Congress:

A, ensure that an appropriate office

within the department has the responsibility to facilitate the gathering and dissemination of national blood collection, distribution, and utilization data, and the development of analytic models to predict shortages. Moreover, adequate Federal dollars should be provided to support collection, analysis, and distribution of these critical public health data.

Specifically, the following actions should be addressed: one, assign responsibility for this activity; two, support programs to develop the data and ensure that the data collected are available to the public; three, encourage collaboration of blood collection centers for the purpose of identifying and addressing areas of short supply of blood and blood products; four, encourage collaboration of plasma manufacturers for the purpose of identifying and addressing areas of short supply of plasma products and the recombinant analogues.

B, support a program of public and physician education designed to improve blood and blood product donation and utilization throughout

the United States and encourage support for such programs through the Department of Health and Human Services.

Such a program was set up within the offices of Blood Safety and Availability Committee within HHS. This enrolled sentinel sites involving approximately 10 percent of the blood collected in the U.S. Steve Nightingale was very instrumental in pulling this together, and a summary of the initial experience was published in Transfusion last year. I believe it was the April Transfusion that had many colorful graphs illustrating the data.

The data collection is ongoing, although there is--it will be restructured as to how the data is analyzed and disseminated. Maybe Mac can comment on that a little bit later.

In January 2002--this was following the 9/11 disaster--consistent with the principles articulated by the American Association of Blood Banks Interorganizational Task Force or Domestic Disasters and Acts of Terrorism, the Advisory

Committee recommends the following:

A, mindful of the needs of all stockholders, DHHS should act to promote and coordinate a single consistent public message on blood issues. The ultimate spokesperson for the blood community should be the Assistant Secretary for Health or her or his designee.

B, emergency support function, No. 8, health and medical services annex of the Federal Response Plan should be reviewed to incorporate the recommendations and organizational members of the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism.

C, the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism should coordinate the national response to the blood community.

D, DHHS should fund the evaluation and potential development of blood reserves in parallel with supporting the development of ongoing programs for monitoring blood availability and shortages, including related reagents and supplies.

And we're going to hear later in the day about the progress that's been made with this interorganizational task force.

In addition, the Advisory Committee recommended that HHS identify blood donors as a critical national resource, promote blood donations as a national service to maintain enough blood on the shelf, to permit rational management of routine needs and disaster responses. It should be a national goal to recognize and promote self-identification of lifetime committed donors willing to donate regularly, at least once a year, and as needed.

The Advisory Committee recommended that the Secretary recognize and incorporate the FDA Office of Blood Research and Review's Strategic Plan into the DHHS Response Plan for counterterrorism and disaster preparedness.

In September 2002, the Committee recommended that DHHS should promote increased public awareness of the ongoing need for routine blood donations by healthy persons via: A,

periodic public service announcements and visible blood donations by top officials and paid advertising campaigns, and to a large extent, this has happened; B, funding of demonstration projects to optimize use of educational and other behavior-influencing approaches; C, supporting specific initiatives to encourage routine donations by young persons and minorities are part of general messages on healthy lifestyle and community support; and, D, play a leading role in increasing participation of Federal employees in donating blood.

DHHS should maintain and increase funding for blood supply monitoring to address: A, long-term trends in blood collection and use; data on daily national distributed blood inventories; C, indicators of blood shortages and excesses; D, predictive models to identify trigger points for coordinated national donation campaigns; and, E, coordination of government and non-governmental initiatives.

DHHS should support initiatives to improve management of blood inventories, including: A,

defining the roles of liquid and/or frozen reserves to, one, moderate fluctuations in supply and, two, to improve disaster response preparedness--and much of this meeting will come out of this resolution; B, integration of supply forecasting into intervention strategies directed to correct imbalances in supply need; and, C, strategies to facilitate movement of blood from area of surplus to area of shortage.

Those were what I thought were the most pertinent recommendations made over the last few years. Any comments or additions from Committee members?

[No response.]

DR. BRECHER: We're running a little ahead of schedule, so I thought we'd just move a little bit further down our agenda because Dr. Beato is not here as yet, and we'll hear our first speaker, Lou Rolon on health sector critical infrastructure protection. Is he here?

[No response.]

DR. BRECHER: Okay. Why don't we go with

experience with reserves. Ron, could you give the Oklahoma Blood Institute experience?

With any luck, we might even finish early today and tomorrow.

DR. GILCHER: I need a little help to bring up my talk. It's on the...

[Pause.]

DR. GILCHER: Concerning conflict of interest, at various times of the year I do receive consulting fees from both Haemonetics and Gambro, and I mention that because I'm going to talk a little bit about the use of their equipment, which we use at our blood center. While we're waiting to bring this us, I'll make some comments.

Our blood center is a large regional blood center. I'm going to show you some pictures that show the area that we cover, and we have a lot of rural areas. We're collecting about 220,000 units of blood products, of which close to about 190,000 are red cell collections, and we use a variety of technologies to do that.

This summer has been probably the most

difficult for us in the last 20 years, and we've had two reasons this summer. One is the post-war Iraq apathy, which I think is affecting the whole country, and we have had an unusually high percentage of deferrals for the variant Creutzfeldt-Jakob disease because of the number of military personnel that we draw or their dependents and retired military personnel who are no longer eligible.

I show you this picture because it's one that none of us will ever forget, and that is the bombing in 1995 of the Murrah Building in Oklahoma City, certainly a day that we will never forget. And a lot of our planning is around this.

Our crisis planning, we operate as though there's a crisis every day. We have the infrastructure, and we can test blood very quickly. But the bottom line is, of course, blood on the shelf. And when you look at the amount of blood that we keep in our system, we have normally about 7,000 units that are active at any point in time. And so when I use--and we need definitions because

we hear that there is only a two- or three-day blood supply in the country, but nobody really knows what that means. So I'm defining it here. That's the total number of units of blood in our system, and in theory that would be about an 18-1/2-day usage. Our plan is to increase that by an additional 2,000 units to take us to 24 days.

The reason for that is that we feel that is the period of time where we could manipulate our system to do additional testing or open up additional test sites or facilitate additional collections or take care of periods of deferrals that might occur from terrorism or bioterrorism attacks. And I'll show you how we're going to do that.

These are our concerns currently: that there would be a terrorist attack that would require large amounts of blood acutely and potentially longer term. The second is a loss of the donor base, and this is a great concern to us. That could be a smallpox exposure or it could be a smallpox vaccination deferral that could take our

donors out we think for period of about 21 days, and that was part of our reason for wanting to increase our blood supply in our own system up to 24 days. And then our third concern is that we could have some for of an incapacitation of our main center, which is where we store about 1,500 units of reserve blood.

Our new plan is to increase our blood availability, as I said, to 24 days, and here we want to use the new frozen red cell technology. And I'm going to talk briefly about that, and our intent is to do this with all Group O red cells. And just as an example, over the weekend we've been very short of Group O red cells, and that is, of course, what everybody wants. We use the new two-unit--it's not new. We've been using it for a long time, but the two-unit red cell collection technology, and we're able to target specifically 135 Group O donors from whom we collect then about 270 Group O red cells. And we did that just at one blood drive.

We have to create some additional

infrastructure to store these 1,000 units of frozen Group O red cells. That is 1,000 in two different locations, and we want to decentralize. I'll show you the map in a moment. And this additional storage of blood which is frozen is going to back up the liquid. The way we look at reserves is that the liquid blood really needs to be the reserves with the frozen back-up to support that. The frozen reserve would be used over a period of three years. That is, approximately 670 to 700 units every year would be incorporated as though they were regular units, and that would be invisible in our system. Again, I'll show you that in a moment.

Then we could also support not only ourselves but theoretically the armed services to whom we put a lot of blood into that program currently, or other places in the United States that would need blood. So the question is how much is enough. Enough in the year 2000, very different from what will be enough in the year 2004, and we think that that difference now is the concern over terrorism and bioterrorism.

Enough means that in our system--and I'm talking now about our system--that all of our hospitals have the amount of blood that they need for availability and transfusion purposes. I think we all realize that blood has two major purposes: that which is transfused, but that which is also available, because that allows surgery, et cetera, to go on. Even if the blood isn't used, it served a purpose.

Then the reserves, liquid and frozen, must be able to handle any major crisis in our system. We do not want to import blood into our system unless--that would be a last resort. And then we must manage the outdating. Outdating is critical because of the high cost of the blood products.

So if you look at crisis in our system, summarizing what I've already said, sudden increased usage, well, we've had two episodes. One is the bombing and then the tornado.

Now, the reality is they didn't use a lot of blood, about 300-plus units within a two- to three-day period, over and above regular usage

during the Oklahoma City bombing, and about 150 units during the tornado. They were very, very different kinds of crises, one very focused, that is, the bombing, the tornado all over central Oklahoma.

Decreased donor availability, as I mentioned before, that is a major concern. That is where the donor base would be exposed to an infectious agent and would not be allowed to donate for some period of time.

And then the loss of blood center functional unit, which actually happened to us, where a wind shear took out one of our sub-centers, totally destroyed it, but it was invisible to our system because the rest of the system, which is decentralized, was able to pick up and supply those hospitals.

So adequacy then, as far as we're concerned, is the availability of enough liquid and frozen red cells--liquid for immediate transfusions, that's the real reserve, and then frozen that backs up the liquid reserves.

Our long-term goal is to move to all Group O red cells, which clearly enhances safety, inventory management, and logistical issues. And that's a whole talk unto itself, and we don't have time for that. Presently that's not possible. But the reality is there is technology in progress that will allow the enzymatic conversion of Group A, B, and AB red cells to O. They're going to be called enzymatic converted, or ECO, red cells. And we're looking very strongly at that technology and believe that that would enhance our system. It certainly would enhance the concept of reserves.

Our red cell stores. With our hospitals, the plan is to always keep--this is the way we currently operate. We keep our hospitals at maximum stores of blood. The inventories are set by both OBI and the hospitals. We decide on what those inventories should be. Then we have a total of six sub-centers in our system. They're each approximately 100 miles apart, and we keep them maximally stocked as well, and they have a core of hospitals around them. This allows

decentralization of our blood stores, and we can move that blood very quickly. And then, of course, we have the main center, which supports, again, a core of hospitals, primarily in the Oklahoma City area, and then is the back-up for the sub-centers and then ultimately all hospitals.

This is what our system looks like, and I think this may put things into better perspective for you. Each of the yellow dots that you see there is what we call a sub-center. The one in the center is Oklahoma City. And if you look at their proximity to Oklahoma City, they're anywhere from 85 to 110 miles away. Each of those stores blood. In fact, at each of those sites we recruit, we collect, we store, and we distribute.

On the other hand, all component manufacturing and all testing is currently centralized. Our long-term plan is to take two of those centers that are about 100 miles apart--I don't have a pointer here, but it's Enid and Tulsa--and put 1,000 units of the frozen stored red cells at each of those sites.

To give you an idea of the number of hospitals that we currently support, we support 92 hospitals.

We support 92 hospitals and an additional 42 transfusion service facilities. We're transfusing about 11,500 red cells per month. That's actually transfused. Our largest hospital transfuses about 1,300 units, and we have about 5 hospitals that transfuse around 1,000 units per month. Our smallest hospital, out in rural Oklahoma, does as few as 6 units per month. And some of those we've already converted to only Group O. That's all we will stock at those hospitals. That really facilitates logistics.

So again, just remembering, comprised under that main center which has all functions, are six subcenters that do not have manufacturing or testing functions, but all other functions.

Really, I've summarized this, but I do want to come back to these points to reiterate that if you look at the blood supply, where it is currently, those 92 hospitals have today about

4,250 red cells. Those six subcenters, excluding Oklahoma City, have about 1,250 red cells. And then our main center--this is our goal--is to have about 1,500 red cells.

We have had difficulty this summer and have been as low as 200 or even under 200 red cells stored, but always maintaining our hospitals and our subcenters, so it's been invisible to our hospitals.

So the total amount in our system then is about 7,000 units. The main center and the subcenter then would have currently, if we're at the goals that we want to be, that is, the 1,500 at the main center, about 2,750 units, which is about a 7-day supply in addition to that which the hospitals have. Their supply is currently an 11-day supply. So we want to generate the additional 2,000 units.

Our objective is to add a frozen reserve to the liquid reserve. The frozen reserve will be integrated into the liquid reserve. The proposed frozen reserve of 2,000 Group O--and we only want

to use O-pos and O-negative units--will add an additional 5-day reserve. That will give us then, as reserves between liquid and frozen, 4,750 red cells or a total of about 12 to 13 days of additional supply. And then of course that will bring us up to about 9,000 red cells, but what that will allow us to do, if you look at the number of liquid units, is that we can mobilize about 1,000 liquid units, and that's the critical point, because we can't mobilize the frozen red cells. I'll show you that in a moment, how long it takes to basically deglycerolize those units. But we can mobilize about 1,000 liquid red cell units within about two hours in our system, without in effect hurting any of our hospitals, and move that to another civilian location within our system, or another place in the country, or theoretically, into the military system.

In looking at the--and I have Lawton here, although we're now looking at Tulsa as the area that we're going to do this--in order to do this, we need technology that allows us to store and then

to deglycerolize--I should say it this way--to deglycerolize a frozen unit and store it in excess of 24 hours, which is where the current technology is. There is new technology, and it uses a device called the ACP-215 system, and the military I believe is currently using this, which allows a unit to be frozen in a closed system and essentially deglycerolized, again, in a closed system, and using an additive solution gives a shelf life of 14 days, and that is absolutely critical to the development of the frozen reserve system.

The 2,000-unit system that we're talking about, in order to buy all of the equipment and basically set that up is going to cost us somewhere between 800 and $900,000. However, when we look at the cost of this, if we distribute it out throughout our system, and we're talking then about turning over this 2,000-unit reserve every three years, so that about 667, theoretically 700 units a year, will be deglycerolized, will then become a liquid unit of red cells with a shelf life of 14

days, will go out to our hospitals, not at a higher price, but at the same processing fee as any other red cell. We think that's critical.

And in looking at that total cost, it will be somewhere between 50 cents and a dollar, and in fact, it's probably closer to about the 50 to 75 cents overall increase for a red cell in order for us to create this reserve system that I'm talking about. And of course the frozen reserve itself will only be Group O, and we have plans on how to recruit donors for that.

Well, the summary then of the new plan is that it's going to take additional low-temp freezers, special blood freezing and thawing equipment, some additional computer systems because of the decentralization, generators to support the power requirements, temperature monitoring systems, and as I mentioned before, our total up-front cost will be between 800 and $900,000. And then we would be prepared to really meet any kind of need within our system or outside the system civilian-wise or potentially even for the military by moving

liquid units, not moving the frozen units.

Now, I want to take just a few minutes--and Mark, I think I have enough time here--to just talk a little bit about freezing. I just want to show you currently some of the disposables that we currently use. You have your glycerol, and you have the disposables that we use to spike the units. But all of this currently is an open system, and it has been developed as a closed system process, and there again you see it.

Here is one of the freezers. These are low-temp freezers that are storing actually at minus 85 degrees centigrade. These don't look very nice, but these are the kind of canisters. We have two of these freezers in our system where we store currently rare units. That is their current purpose.

Here's what the unit of red cell looks like in our system when it's frozen. There are other systems that have been developed. Dr. Volare's laboratory has developed a different kind of packaging system. And of course the labels have

to be there.

This has been the workhorse. This happens to be a device that was originally made by the IBM Corporation, and then IBM was acquired by Gambro, and it's a device that we use for deglycerolyzing red cells. We have used this for many years. There's another device. This is a Haemonetics device. These are the older system.

The problem with them is that the deglycerolized unit has only then a 24 hour storage, and that makes it extremely difficult for us, or even for the military, to use these units of blood in that period of time.

This is a new system that has been approved--I believe that's correct, Dr. Epstein--by the FDA, which uses an anticoagulant called CPDA-1, an additive solution, and then allows, as long as it's using closed system technology, to store the unit of red cells for 14 days. This is the type of system that we intend to go to.

The problems--and I've just outlined them here for you--in the past and present is that we've

used open systems, that's a 24-hour out-date, the freezing time, deglycerolization time, is basically an hour on the front end, an hour on the back end. So you'd have to have a lot of these devices to thaw a lot of blood in a hurry. We don't need to do that the way we've planned it. We would have somewhere between six and eight devices, three or four at each location, because liquid blood is our true reserve for immediate reserves, and this is our more long-term backup.

Then of course the long-storage concept is good for military and rare units. The high cost and high out-date has been the problem with the 24 hour out-dating.

The needs for the future. Closed systems, we're there. Additive solutions for longer post-thaw storage, and we've got that. But we don't have the right anticoagulants as I'll show you in a second. I think that we need to rethink the strategies for use. That is, we've talked about using the frozen red cells for emergencies, but in reality they're too hard to deglycerolize in a

hurry. We need to look at the liquid red cell inventory, have an adequate amount of that to be the immediate backup, and then be able to consistently deglycerolize the units and move them into the system, and they need to be all Group O.

Summarizing, the current Haemonetics ACP-215 system--and obviously it's one of the things that I talked with Haemonetics about--the advantages are: it's a closed system; it uses an additive solution; and it has a shelf life of 14 days for CPDA-1. That's in fact a disadvantage because we don't use CPDA-1, and it's hard for us then to just do a CPDA-1 drive and move that blood specifically for this purpose. We use CPD and CP2D, and currently there is work going on to license those anticoagulants. That will make this system far more effective for us.

Other future uses for the frozen red cells of course are to couple them with the double red cell procedure collection technology, and there are now two companies that have devices that can do that, and as I mentioned to you, we have used that

now extensively in order to enhance our red cells and specifically our Group O red cells. And then support liquid red cells at times of high liquid usage, and then incorporate into routine use--and I think that is critical--for the frozen red cells to be used. If we want to charge them out at 200 or $250 plus per unit, then they won't be used. But if we incorporate them into our system as, quote, "as though they were a liquid red cell unit," we will end up having them used.

That is a fast overview as reserves as we plan to do that, what we are currently doing and where we are going at the Oklahoma Blood Institute. I'll be glad to take any questions.

Karen?

MS. LIPTON: Actually, one comment quickly, and that is that we've focused on supply here, but the other advantage to that Group O is really elimination of errors and accidents in the transfusion service, which I think could be very helpful.

DR. GILCHER: Absolutely.

MS. LIPTON: I just had two quick questions. Number one, when I look--in your testing capacity, if you could address disruptions to testing capacity, because that would seem to be a limiter. And then the other question is, how do you deal with the changing--as you're rotating in the frozen, how do you deal with the changing donor suitability requirements? Are you defining a certain type of donor that you actually put into the frozen inventory? How do you deal with that issue?

DR. GILCHER: The testing issue is a concern because we only test in one location, and that's a critical location. We also do all of our component manufacturing, because we really are a manufacturing facility, at one location. We could set our manufacturing up in other locations as long as we had the space. We could move it in that three-week period of time. Testing would be very difficult. We would have to find an alternative source of testing, and hopefully that would exist. That would be very difficult for us to set up.

The second question was?

MS. LIPTON: The donor suitability in rotating the frozen units.

DR. GILCHER: When we looked at how long we could store these units and how fast would we have to turn them over, initially we thought four years, but I think that three years is more realistic with the various changes that are coming along. Some would require that--in theory those units have to be tested. Our plan is to keep a repository sample frozen of plasma from every unit so that we can do additional testing if that was a critical test or deemed a critical test, in order to release those units.

MS. LIPTON: And then you wouldn't--but in terms of donor suitability, if there were other requirements put in in terms of collection of units from donors that have now become at risk for something, you wouldn't do any additional screening of that?

DR. GILCHER: Of course we don't know what to screen for at this point in time, and we'd have

to be able to get around that issue because the donors would have been drawn at a time when they would have been acceptable.

MS. LIPTON: Right.

DR. GILCHER: And then the question is, are they not acceptable because of something that we find out in the future? That's a hurdle we'd have to cover.

Jay?

DR. EPSTEIN: I have two questions, Ron. Also, thank you. This was really a very helpful oversight.

Do you have any comments about the need for platelet reserves and any strategies to deal with platelets? That's the first question.

And the second question is, could you comment on what it takes in terms of resources to have any significant throughput when you're thawing a frozen unit? In other words, how many units can one technical with one machine prepare per day?

DR. GILCHER: I didn't comment on platelets or plasma, one, because there isn't that

much plasma used. We do keep a lot of reserves on plasma. Our concept on platelets, Jay, is that we believe that the platelets will have to be stored in the donor, and that we have to have a core of donors upon whom we can call. We've looked at doing certain things with some of these donors.

For example, we're trying to find donors in our system who have been vaccinated for smallpox. And then talk to them about being a donor because that is one of the concerns in the future. If we had an attack on a country where smallpox were introduced or we had to do mass immunization, we need a core of donors who really are already immunized. We're trying to think ahead in that regard, but we think that platelets really have to be stored in the donor, and we have to then be able to call on that core of donors at that particular point in time.

The second part of the question was the throughput. It's basically an hour per machine. We work around the clock in our system, in our component manufacturing areas. And we would be

able to, we think, with three devices at each location, which is a total of six devices, we could do about 20 units per device per day, running around the clock, and that allows a little extra time for mishaps. So we could basically deglyce about 120 units of the frozen per day--now, they are Group O--to put back into our system. We think that that would be enough. If not, we can increase the number of devices, but it's basically 20 units per device per day, and that's using it--

DR. EPSTEIN: If you have the staff.

DR. GILCHER: Yes, we have to have the staff to do that, right.

Gerry?

DR. SANDLER: I'm Gerry Sandler, and I'm here representing hospitals actually, and I was marveling at how well you've selected from the technology. But what I was really focusing on is, here we go again with another very attractive program that's being built on, the add-on to the patients who are in the hospital today, who have got nothing to do with the need for the reserves.

We would be giving--with the way you described, a 50-cent to a dollar tag on a bill to current patients, and giving the United States Military and Homeland Security a free ride, by getting their insurance and the reserve.

My question is, is there anything intrinsic to the concept that wouldn't be consistent with a proposal that Homeland Security and the military build a national reserve of frozen blood, on your model, and if in times of crisis the hospitals had to tap off that, they could pay as they go?

DR. GILCHER: Well, the front end costs that I've talked about here--and that actually is the cost of bringing that first 2,000 units into the system--we've already approached the Homeland Security issue in Oklahoma. There have been monies given by the feds to Oklahoma, and none of that money has been tapped so far, not a dollar of it, and that's because there have to be state matching funds and the state doesn't have the funds. But what the state has told us, if we can go out and

raise the matching funds, have those given to the state, the state will allocate them, and so we will then be able to access that. We're working on that. You're right. That is one of the ways that we can help to pay for it.

Otherwise, it does have to come out of operating costs because nothing is free and we have to pay for this.

Harvey.

DR. KLEIN: Harvey Klein. Ron, since you're targeting a certain group of O donors and since your frozen reserve is not something that you're going to use for unplanned emergencies, it seems to me that you might be able to contact these individuals should additional donor qualifications arise, such as geographic exclusions. Are you making any plan to do that kind of requalification?

DR. GILCHER: Yes, that's a good point. The donors that we intend to target are going to be the regular donors in our system who are donors that we can get back in case the frozen repository sample wouldn't be adequate or we needed additional

information, if that's what you're driving at.

DR. KLEIN: I am, but I don't even think you'd have to get them back. There are lots of ways of communication to find out if they lived in Europe in the last 20 years or some other such new qualification requirement.

DR. GILCHER: Right. We don't want to target donors that would be potentially deferrable, if you understand what I'm driving at.

Dr. Heaton?

DR. HEATON: Andrew Heaton. Ron, could you comment on the loss of red cells during the freezing, thawing and deglycing process? What do you actually recover at the end, without the storage loss? And then secondly, comment on the cost of a standard unit of red cells versus a thawed, deglyced red cell?

DR. GILCHER: It's a good question, Dr. Heaton. The way the system is currently set up, it really is set up for a 450 ml red cell collection, and there have to be some modifications so we can really maximize the red cells, because there is

some loss just because of the way the current systems are set up, because we essentially do a 500 ml whole blood collection.

What we target in our system is 200 mls of absolute red cell mass per collection. That is what we're targeting out of a 500 ml whole blood collection, and currently when you freeze a unit, what you end up actually freezing is around 180, maybe 185 mls of absolute red cell mass with approximately somewhere between a 10 to as high as a 20 percent loss during the deglycerolization procedure, which is partly hemolysis, but also some red cells that are lost as whole red cells.

DR. BRECHER: Ron, we're going to have to conclude this one. Thank you very much.

DR. GILCHER: Thank you.

DR. BRECHER: We're now going to return back to our schedule, and I'm very happy to introduce Dr. Christina Beato, who is the Principal Deputy Assistant Secretary for Health.

DR. BEATO: Good morning. Like Dr. Brecher said, my name is Christina Beato, and I am

now the Acting Assistant Secretary for Health. I want to welcome you all here this morning, and on behalf of President Bush and Secretary Tommy Thompson, sincerely thank you for all the work that you are doing on behalf of trying to give us your best expertise and ideas on how we can create policy to meet the variety of needs that our nation is facing, and hypothetically, will continue to face in the future.

I come from the state of New Mexico, Albuquerque, New Mexico. I'm one of the new westerners here in the D.C. area. I am fascinated by the D.C. culture, but certainly miss the desert Southwest, and just wanted to say a little bit about myself in that sense that this is a beautiful country, but I still say that the Southwest beats you all.

[Laughter.]

DR. BEATO: My last two years at the Department of Health and Human Services has been an incredible experience, and I have learned a lot about your Committee, worked very closely with

Mike, and had the pleasure to meet your chair, three or four months ago? About two months ago.

So I'm quite familiar. I come from an academic medical center as well as the only Level I trauma center in the State of New Mexico. So the issues of blood, blood transfusion, errors. And also from a state the has Los Alamos, Sandia, and the home of the Stealth fighters, Clovis, New Mexico. So we work closely with military units as well. I can tell you that this is an important critical topic, not just in every day issues with hospitals, trauma, chronic diseases, congenital diseases, but also facing our new environment of BT.

As the Acting Assistant Secretary I look forward to working with you all to make blood more available, and in these uncertain times, making it as safe as it's reasonably possible to do.

Last year, Dr. Eve Slater, the previous Assistant Secretary for Health, spoke to this Committee on several issues. In particular she asked you to consider the maintenance of an

adequate blood supply in the face of mass smallpox vaccination at a future meeting. Smallpox is a particular specific issue, but there are other agents that could create a situation where the blood supply could be drastically reduced and demand increased. I'm going to ask this Committee to sort of broaden away from just looking at small pox. I'm going to ask you to really look at a broader picture, at a systems issue, so that we can get your best advice in a more comprehensive manner.

For example, in our country today we're experiencing the West Nile epidemic. China and Canada, since you last met, we experienced SARS. Canada has a BSE case. It's our neighbor very close to the north. The trade with the meat in this country is very, very tied in together. This is a situation that could possibly influence our supply and demand in both countries.

The U.S. has experienced something called monkeypox, which was unheard of in the Western Hemisphere. There are new emerging infectious

diseases in our hemisphere that we predict will continue to do so due to global mobilization, the way folks move in and out. Agent TTVX could be discovered that affects our blood supply, and needless to say, what's always in the back of our heads, another event of bioterrorism.

While BT is clearly an unnatural event and potentially quite devastating, the real threat occurs every day, and I know this being an ER doc and working in a trauma center. Due to the variety of situations that could reduce the blood supply, or increase demand on a daily basis, I think it's quite important to consider the scenarios beyond a BT event.

As my friend, Dr. Brecher has already reviewed, the Committee has made recommendations regarding reserves. I want to ask you again today to take a broader, more comprehensive and thorough than you have in the past, a look at that issue again.

Again, I'm sorry I'm late. We were in a car accident. They wanted to haul me off to the

hospital. The car did get totally crunched. But I thought it was quite important to come meet you and say hello to you, and ask you to look at this, because these issues, even as new BT dollars get allotted, indeed they will go through Homeland Security, but our Department is in charge of stockpiling. We are in charge of collaborating with the Commission Corps, and working together with De-Mat teams. So this is going to be an issue where we certainly will continue to have a lot of influence and certainly create the policy surrounding that.

So again, on behalf of my boss, Tommy Thompson, and President Bush, and during all these exciting and challenging times, thank you very much, and I look forward to hearing what you all have to say when you get done.

Thank you.

DR. BRECHER: Thank you, Dr. Beato. You have time for maybe a question or two from the Committee members?

DR. BEATO: I do. I'm already late, but

I'll be glad to take one or two.

DR. BRECHER: There may not be any.

DR. BEATO: Any questions?

[No response.]

DR. BEATO: Thank you so much.

DR. BRECHER: Thanks a lot.

Okay. We're a little ahead of schedule, so we're going to take a break, and we'll come back at 10 o'clock and that will put us back on schedule.

[Recess.]

DR. BRECHER: We are going to resume. We're trying to get back on schedule here. The next talk will be the Health Sector Critical Infrastructure Protection, Lou Rolon.

Thank you.

MR. ROLON: Thank you. Good morning. My name is Louis Rolon. I work for Logistics Management Institute out of McLean, Virginia. I'm the functional expert for CIP, for the develop of CIP. Over to my right here is John DiDoro [ph]. He's the technical led for LMI on the CIP

initiative for the health sector.

We were invited to come here and speak to you all. Captain McMurtry I believe received a briefing from my boss recently, and he asked us to come down here and give you a brief. Unfortunately, my boss couldn't be here. He had to go on vacation for a well-deserved rest. And I'm here to provide you a general overview of the critical infrastructure program or protection program and how it relates to the health sector.

What is CIP? Many of you may have heard this term, and essentially what it is, it's the identification, the assessment and safeguarding of critical assets whether they're physical or cyber, and any associated infrastructure that is essential to the execution of the DOD mission.

Bottom line with CIP is mission assurance. That's our goal. CIP is a comprehensive process that allows you to understand and protect the critical assets, or the assets that are critical to our national security during peace, during war, or during any crisis. If I can digress a little bit,

you may have, many of you, heard what happened about a week and a half ago with the power grid. That was a classic example of CIP. You heard on the radio people talking about critical infrastructure, about risk, about vulnerabilities, about coming up with strategies to deal with fixing and minimizing the risk to the critical infrastructure. That was all over the radio, and this is what it's all about.

In essence, CIP has a life cycle of its own. It starts with identifying the items, and it goes all the way through, if it needs be, to reconstitute the critical asset if it gets compromised. I'm not going to go into each one of these, because it could take an hour to discuss each one of them and I'm not prepared to do that.

This is the DOD organization. I will tell you that the part that you need to know here is--right here are the sectors within DOD. There's, I believe, 10 here, the health sector being one of them. And we basically report up to the Secretary of Defense. The DOD CIP recently was switched from

operational control of C3I to Department of Homeland Security, which is a good move in our view, in terms of support, in terms of resources.

Within the DOD organization you have the Health Sector. We report to Health Affairs. At Health Affairs we report to Ms. Embry, who's our boss. Within the Health Sector we receive operational technical support from the Joint Program Office. Also within the Health Sector is divided into 11 categories. We're only showing 8 here and the only reason why we're showing 8 is because these are the areas of emphasis currently ongoing. As you see again, we have blood. Currently we're in the analysis and assessment phase. What this means is we're trying to identify the critical assets within the health sector, want to identify the risks, vulnerabilities, and then we want to be able to identify what actions we need, what strategies we need to minimize or prevent those risks.

What this kind of shows is within the Health Sector we have the PHAST database, which

stands for the Primary Health Assets Staging Tool. That's the database that we're currently developing that identifies the critical assets within the health sector. We do data dumps to the--staging tool down at the Joint Program Office in Dahlgren, Virginia. They in turn, that information gets validated. It can be manipulated. It gets integrated into this process, into the CIP database at the JPO.

Now, within the JPO they have this visualization tool called the Operational Dependency Information Network. And I'll show you what that capability is in a second here. The JPO has a very powerful visualization tool that allows you to depict critical assets for any given scenario there may be. For example, let's take blood. We identify blood assets. Using the visualization tool, using what they call CROP, which is I guess a GIS type of application, they can depict these blood assets anywhere throughout the U.S. or overseas.

If, giving you an example--I'm kind of

getting some blank stares here. If for example, something happens in D.C. concerning a biological/chemical attack, this product can depict the contaminated area. It can show those critical assets that have been compromised. It will show those critical assets outside the area that the medical response teams can use to move patients or move casualties to those critical assets. It will be able to show what capabilities those assets have. So if it's a trauma center, if it's a medical center, whatever it may be. That's where they're headed with this.

Our health sector objectives are divided into two categories. We're talking at the tactical operational level, essentially what I've been talking about, is to develop the--identify the critical assets so that we can get that integrated into the JPO database. And then we have the strategic, and that's developing the strategy, what we call the Defense Infrastructure Sector Assurance Plan, the DISAP. We'll talk about that in a moment, in a few slides, in a moment. That's

essentially the road map. That's a strategy for how we're going to get from point A to point B in the health sector CIP process. It's kind of hard to see.

This is a little bit dated. For those of you that are very observant, if you compare this slide with the previous slide, where it showed the health sector organization, there are a few differences. But what I wanted to convey here, in order for us to get here, we need the functional support from the capability areas so that we can get the information that will flow through into the PHAST and into the JPO database.

I highlighted blood here, kind of give you a feel for what we're talking about when it comes to analysis and assessment. Within the blood sector, you'll see that we identify the assets, we identify the attributes of those assets, capabilities. We identify vulnerabilities to those assets so that we can again protect and minimize any compromise of those assets. We talked about the DISAP. Essentially that's our road map to the

health sector CIP process. It's going to be a major document that essentially delineates how it is we're going to do things.

We have the establishment of the Federal Healthcare CIP Working Group. That brings together all the capability area experts, blood, medical facilities to plug all medical units on and so forth, into an environment where we can sit down and discuss the strategy. This is ongoing as we speak. We plan on holding our first meeting sometime in September. We are having a subsector meeting with the Armed Forces Blood Program Office on the 12th of September, in fact.

What I want to do now is kind of give a quick demonstration of the PHAST. We're essentially in the beginning stages of the development and design of PHAST. I'm going to show you the initial database design was kind of a dinosaur type, but it's not very intuitive. Then I'll show you where we're going in terms of the new database design.

What we want to do within PHAST is build a

foundation. We want to know who it is, where it is and what does it do. That's all we're trying to do. We're trying to lay to first foundation, layer of foundation, of this process. We're trying to build a house, building the foundation. Then we'll start building on top of that.

This is what PHAST looks like. This is what you'll see initially on the screen. Many of you who don't have the briefing packets, it identifies the asset, identifies where the asset is, has a long identification, and it has other information that you can put on there. You can add some information in terms of what that asset can do. I have, for example, some assets within PHAST that may have a capability that I have to add within the functional code area down there.

Any questions before we get into--none?

DR. BRECHER: Jay?

DR. EPSTEIN: On your 11th slide under "blood," part of the assurance plan, you mention strategic national blood reserve. Were you going to elaborate on current thinking in that area?

MR. ROLON: Well, I'm not in a position to do that. These were things that my boss--he's the strategic mastermind of this--what he was thinking out in his mind, what might be areas that we need to discuss as we develop and structure the blood capability area. It's not confined to what you see there. As we meet with the blood subsector, they will assist us in identifying what that will be in order for us to development the DISAP.

Any other questions?

[No response.]

MR. ROLON: If you'll bear with me a second.

[Pause.]

MR. ROLON: The staging tool that we're using right now gives you information concerning what it is, where is it, and what does it do? That's essentially what we're doing now. What it provides is we have physical assets that we're trying to identify right now. Those are the critical assets within the capability areas.

And just quickly to go through this, we

can do general searches, and I'll do a general search concerning the capability area, in this case being blood, and it should give me the information that I've currently been able to gather and integrate into the database.

Now, let me take one here. Let's take the 10th Medical Group Transfusion Service, and it brings up the information concerning that asset. If I hit "capabilities," it gives me right now the capabilities that we've identified--I hope it does. It's kind of slow here. It looks like I have a duplication here, but essentially the transfusion service, to my understanding, is that it provides storage and transfusion services. We still have to do some data cleanup as we go along, and as we sit down with the blood capability area, we'll define that even further.

We also have point of contact information. Again we have a duplication here. We also can provide images. We don't have images at this time. We hope that in the future, down the road maybe a year or two out, we can provide image information

on that facility or that asset.

Right now we don't have anything under "sustainabilities." In fact we renamed this to, I believe, "vulnerabilities," and we'll show you that in a second.

This is what the new version of PHAST looks like. It's very intuitive. It allows you to get in and out of screens very easily. The previous one I just showed you does not. It's a very cumbersome, very tedious process you have to go through in entering data, and it takes a while. So we've developed this new version. It's going to launch here in about two weeks. It will allow whoever uses it the ability to--in other words, it's very user friendly is what I'm trying to get at.

Any questions to this point? Yes, sir.

DR. HEATON: Andrew Heaton, Chiron. Is it the intention of the agency to better document maximal throughput of production or capabilities rather than just physical assets? This database looks like a physical asset description. It

doesn't describe capability, and is it their intention to do that?

MR. ROLON: It will identify capabilities. That is the essence of this database is to identify those capabilities. Right now, remember, we're laying down the first layer. As we grow, those capabilities will be identified. As we sit down with the capability areas, they will assist us in identifying what those capabilities are going to be, what the vulnerabilities are going to be. We'll identify that. That will go into the database.

DR. HEATON: And you'll extend this to cover civilian agencies as well as military.

MR. ROLON: We're very dependent, the health sector if very dependent on the commercial and private sector, so my answer to you will be yes. But the initial goal is to identify the DOD assets, not within blood. Obviously you're very well integrated with the commercial side of the house. So we understand that. We've been working on that as well.

DR. HEATON: Thank you.

MR. ROLON: Any other questions?

DR. BRECHER: What do you mean by vulnerabilities or susceptibilities, say in the context of blood? Could you give a few examples?

MR. ROLON: We're talking about those things that can compromise the asset and its ability to function. So if, let's say, within blood you have things that sustain blood, power utilities, supplies, whatever it may be, that is a vulnerability. The power can be a risk. It can be a vulnerability.

DR. BRECHER: Any other questions? If not, okay, thank you.

MR. ROLON: I want to thank you all for inviting us down, sir. It's a pleasure.

DR. BRECHER: We're going to move back to discussing reserves, and we're now going to hear from the Department of Defense, Brenda Bartley.

COMMANDER BARTLEY: Good morning. I was asked to come down here this morning to give you a brief overview of some of the experience that the

Department of Defense and the military has had with frozen blood and frozen blood reserves, so I hope to do that this morning.

Just to give you a little bit of a background, the reason that we established a frozen blood program to begin with is because in--normally in peacetime--of course we have a little bit more blood on the shelf right now than we normally did--but normally we only keep about 700 units on the shelf that's available to ship overseas for a no-notice conflict, and we estimate that it would take us a minimum of 72 hours from the time that we activated our blood donor centers, till the time that the first units that are collected are available to ship. So we have a little bit of a lapse there in between the time that blood may be needed and the amount of liquid blood that we have on the shelf.

So back in the late '80s, early '90--the military's been freezing blood for about 30 years, specifically over the last 20 years--but in the late '80s, early '90s, we began to start freezing

large quantities of blood products specifically to preposition in frozen blood product depots worldwide and on hospital ships and naval vessels in order to have that stopgap solution until liquid blood was available to flow into our hospital areas. And it was also used within the medical treatment facilities and our hospitals in CONUS in peacetime, to supplement our inventory with O-negs. Back before, during the Cold War, we had about 225,000 units of frozen blood prepositioned worldwide. And since the world has changed so much lately, our requirements have decreased. So currently we have an inventory of about 61,000 units, and our distribution of O-pos, O-neg, you can see there is 85 and 15, is what we try to do.

Basically here's the distribution of where we keep our frozen units. Most of it is in the Pacific, as you can understand, a little bit in Europe, and within CONUS we have some frozen within different hospitals and aboard naval ships.

The CONUS depots we talk about is our armed service whole blood processing laboratories

that are Air Force facilities at McGuire Air Force Base and Travis Air Force Base in California. McGuire is in New Jersey.

And you can see we do put frozen blood, and currently have frozen blood board our naval vessels that we have casualty receiving and treatment ships. They can hold up to 950 units, and our hospital ships can store upwards of 3,000 units. We don't always keep that amount on board, but they do have that capability and storage capability.

So our blood product depots worldwide were built, like I said, in the early '90s, and we have a blood product depot in Okinawa, and then we also have two in Korea, and there's one in Sigonella Sicily, so that just shows you where our assets are. And those blood product depots, their function is to receive and store frozen blood, and then if they're activated 24 hours a day, they would be deglycing that frozen blood and making it available, and we estimate that it would only be working for about 10 days. Of course, you don't

want to be deglycing frozen blood once liquid blood starts flowing in because it's so time consuming. And then our job is to distribute that frozen, deglycerolized blood to the field hospitals where it's needed.

There's a bad picture of the blood product depot, our newest one that we have in Okinawa there. It's a 60,000 square foot facility that was just recently built in about--about 10 years ago. You can see the massive amount of freezers that are in there. I think we have 20, 25 of those ultra-low freezers with the double compressors. They also have CO 2 backup systems, and then we have emergency generators so that the facilities are set up in order to--we have multiple power failures in the Pacific with typhoons.

In the left-hand side you can see we have the old Haemonetics 115 cell washers, and there's about 30 of those, and there's a big water bath to thaw the units out. So there's a huge equipment outlay that's required for frozen blood.

So in the old methodology that we use, we

still use the high glycerol, 40 percent weight to volume method. That hasn't changed as Dr. Volare's method. But the current units in inventory that we have now are collected in CPDA-1 in the 800 ml collection bag, and we freeze in that primary bag. The age of the red cells when they're frozen, you can see are six days or less, has to have a very specific hematocrit range, and I put a few of the steps that it takes basically just to show you that it is very time consuming, it is very labor intensive, all the steps that need to go through, all the very specific things that have to be done to the unit, and it takes about, by the old methodology--when I say old methodology, that's using an open system--it takes about an hour to freeze a unit of red cells. Now, you can do those in mass quantity, and you can probably freeze 10 at a time, but it does take some time. They're placed in the bottom of a minus 80 degree freezer, and it's supposed to be within four hours from the time that you take it out of the refrigerator.

So the main thing is they have to be less

than six days old. You have to warm them up, and then it takes about an hour to prepare them before they go into the freezer.

The Haemonetics cell washer is the methodology that we have out there. We have hundreds of these deployed to different medical treatment facilities within the United States and overseas in all of our blood product depots again.

My red didn't show up very well. Basically, the point that I was trying to emphasize here is that we only have a 24-hour, as you know, post-thaw shelf life on these units because it is an open system. They're manual, so we have a lot--I think a lot of error. We have about a 15 percent breakage hemolysis rate when we deglyce these because you're manually adding the saline to it, and if you don't do it exactly right, you hemolyze the unit. The thaw time, it takes about 30 minutes to thaw these units out in a water bath.

Now, the throughput on this is we can't do this very fast. It's all dependent on the number of machines that you have. So you can produce one

unit per hour for every machine. So if you have 30 machines, you can produce 30 units an hour, and that's it. We have done multiple, multiple time-phased studies on this and we know that this is a good number, even with very well trained technicians. And one tech can usually handle two, maybe three machines at a time, so it's slow. It's not something that you're going to be able to produce massive quantities at one time, but we--that's why we put a lot of cell washers and we planned on operating 24 hours a day.

The preservative solution you can see that these units are suspended in is .9, .2 saline dextrose. The problem is that the Haemonetics 115s are not being manufactured any more. It's hard to get replacement parts. So we were very anxious to get a new instrumentation that would help us out.

The Haemonetics 215--and I understand you're going to have a presentation later on from Dr. Holmberg, so I won't go into a lot of detail on this, but I did want to touch on it. We were very excited when this machine came out and when it was

approved by the FDA because it is automated. It's process controlled. It's FDA approved. The units are sterile docked. It's a closed system technology and it's approved for 14 days post-thaw shelf life, which is exciting for us, because that increases our availability of red cells at remote locations, and it also helped us reduce the frequency of having to resupply small field hospitals, when we can put blood out there that's got 14 days on it after deglycing it. The throughput, again, it still takes 30 minutes to thaw a unit in a water bath. The throughput, it's a little bit faster--not faster--it's a little bit better in the fact that it frees up personnel. One person can operate three to four machines instead of one to two machines. But we still have about one unit per hour per machine. So again, you're machine dependent on the time that it takes, but one person can't operate more, so you've saved some labor.

That's just a slide that you can look at and see--we were excited about the recoveries. The

hematocrit it good. The hemolysis is very low, and the potassium, after 14 days of storage. So the military was very excited when this came out.

So the other thing that we are excited about is this new plasma thawer, and we understand that it is now--has now obtained FDA approval for thawing frozen red cells, and that helps us in that the water bath issue was--you know, the units would break. It would contaminate. So we're very excited about being able to use this. It's got membranes down in there where you can get various size bags.

Another instrumentation that's out there that is not approved but is still under development, and the military is following very closely and is helping to front some of this research as mission medical. It is a hollow-fiber filtration technique. Also they are looking at 14-day post thaw. They use a dry water bath though in the throughput. This is what the military is excited about. It's supposed to be one unit per 30 minutes per machine, so this could cut down our

processing time in half if in fact it comes to fruition. Same amount of technicians and machines.

They have a new trademarked bag they're calling a Stericon bag, which is a lot better, a lot more resistant to breakage, and it also preserves the red cells just like the Haemonetics and the AS-3. The recovery is very similar. As I mentioned, the freezing bag is flat, and you can see at the bottom the dry thaw bath that they're proposing with their system can reduce your thawing time for 7 minutes if you're using the Stericon bag to only 13 minutes if you're using the 800 ml bag.

So this, if it comes about, could really speed up our production. That's just a comparison chart of what I just mentioned.

So now, our challenges. So we are very excited about the system. The regulatory constraints that we're facing now though is that we have these 60,000 units of frozen blood that are out there. I think one of my slides didn't come through, but basically the problem with the frozen blood out there today is it's very hard--you can't

keep up with all the changes and the questions, and the donor screening requirements and the testing. So we really need to replace the units. And we have a lot that are coming to the 10-year expiration, so we really need to replace the 60,000 units that out there, and so in setting up our modernization plan to replace that, these are some of the constraints that we've come across.

The current Haemonetics 14-day post thaw ACP-215 is only approved for CPDA-1 collected in the 800 ml bag. Well, of course, very few people use that bag any more. Military still collects in it some just specifically for this reason. And so additional studies are going to need to be done for AS-1 and AS-5. Our understanding is that some of the blood industry is doing some current studies for the AS-1 anticoagulant to collect the blood in the AS-1 anticoagulant, and the military is looking at doing some studies with Haemonetics too on the AS-5 anticoagulant. So what we really want to do is move away from this 800 ml bag and use a primary freezing bag that's sterilely docked, and then use

other anticoagulants, because the rest of the world collects in AS-1 and AS-5 also.

The other issue that we're currently discussing with the FDA is the approval for this is only for storage at minus 80 degrees centigrade or colder, and as you know, currently the current methodology is approved for minus 65 degrees C or colder, so we're in discussion with the FDA trying to get this resolved, but we may have to do additional studies to prove that the minus 65 degree or colder storage is equivalent to the minus 80 degree. They say they don't know whether the good recoveries and post transfusion survivals are due to the storage at minus 80 or whether it was equivalent at minus 65. So we may have to do some additional studies, but we're working with them on that. So that's a big constraint.

We're not sure whether we're going to be able to take our old units and use the automated system and deglyce the old units on the new machine and still have a licensed product, even though the technology didn't change, it just automated the

process. So we're working with the FDA to resolve that.

And then there is a big question regarding 3-year versus 10-year storage. The CFR currently has minus 65 degrees for 10 years for frozen red cells, but again, the question is going to come up as to whether when we apply for our licensure, whether we're going to get that 10-year storage because they don't have any units that have been stored, frozen and stored by the new methodology for 10 years and deglyced to prove that it's equivalent, but hopefully we'll be able to use some of our older data to show that it is.

The shelf life issue, the minus-65-degree issue, the main problem with frozen blood reserve is that any blood that you freeze, as soon as a new question comes out, you know, as soon as a new donor screening procedure comes out, your units are not going to meet the current FDA guidelines for donor screening or donor testing. And as you can see, there's numerous tests that have come out over the last few years. So that's a big problem.

Logistical issues with the new instrumentation, it's a small--the wash bowl needs to be a little bit bigger. We're going to do some studies on a bigger wash bowl, but because of the current wash bowl, you have to adjust your collection sizes. You have to make sure that the hematocrit is not greater than 46 percent. So it's not something you can't overcome, but you just have to make some adjustments and be very careful in collection in your donor hematocrit and hemoglobins.

In addition to that, shipping frozen blood is very cumbersome, dry ice, and 30 pounds of dry ice and you can only put about 16--we put about 16 units of blood in a box. That becomes very expensive and very hard to re-ice if it's going to be longer than 48 hours and you're shipping long distances like we do. Again, I mentioned the water bath is definitely a limiting factor. As soon as you throw a couple of units of frozen blood in a water bath, that temperature goes down so low that it's hard to thaw the units out. So that's why

we're very excited about the thermogenesis machine.

Logistical issues in a frozen blood reserve program. You have to look at--when you freeze it, you can't freeze it all at once. This is a lesson learned for us. We froze several units over probably three to five years, and then now all of our units are coming very close to expiration. So you have to set up a plan so that your frozen blood is frozen over a seven- to ten-year period, whatever the expiration date, shelf life of those products are.

And then people talk about, well, why don't you just rotate your products? Why don't you rotate your reserve and then freeze every year? Well, if you look at what it would take--and I've got some cost estimates there that later you can see--you would have to constantly freeze every year to replace your expiring units, and then you'd have to use them during peacetime. You have to be using your frozen units; otherwise, you're going to be throwing them away. And then there are costs that are associated with deglycing, additional

deglycing. So it's really more costly to freeze and deglyce a unit than it is to collect--or to deglyce a unit than it is to collect the red cell. So, subsequently, we have not rotated our units, and we just can't use them all in peacetime. And so that's why they're expiring.

An additional thing to think about is you've got frozen samples that have to be kept. Well, at first we didn't keep frozen samples. Then we got smart and decided we were going to keep them. But then we collected--we had little cryovials with serum or plasma in it. But then we decided we were going to put them in the box. And then when HIV-1 antigen came out and we had to go back and retrospectively test all the units, we had to go open up every single box to pull out these cryovials. So definitely a lesson learned is you have to have your serum samples or your frozen samples for retrospective testing has to be centrally maintained in a database so that one or two places will have the specimens and can do the testing and not have them located with the units.

It's too logistically--too much of a problem, which we found out.

The samples also nowadays with NAT would have to be PCR quality. Well, the samples that we've saved are not PCR quality. They were serum and plasma that were pulled off of the testing tube when we frozen the units. So, subsequently, we can't test these units for HCV and HIV by NAT.

Then, also, with the NAT technology, you have to remember that you have to document the multiple-sample freeze-thaw cycles. If you take them out to do a new test, you have to document when you took it out, how long it was out. So there's a lot to think about when you're setting up those frozen samples.

Some cost factors for you to consider. This is what we have estimated it would take us to replace the inventory that we have, so that's what this is based on. If you look at it, we estimate that it costs about $415 to freeze a unit, and that includes everything--collection, testing, equipment, personnel--and then about $85 to thaw

and prepare.

In addition to that, the instrumentation, you know, it probably has a shelf life of seven to ten years, I think, I would estimate. So we estimated a ten-year--not shelf life but equipment life, maybe less than that. So every ten years or so, you're going to have to replace the instrumentation. Initially you've got to freeze the unit, so we figure it's going to cost us about $28.5 million over a ten-year period just to build up--we've decided we want to freeze 68,000 instead of the 61,000 we have because we have some additional ships out there.

Then if you're going to use it during peacetime to rotate it, at $85 a unit to deglyce it, then, again, that's another $500,000 that it's going to cost us if we use the units in peacetime, about 10 percent per year. So basically you're constantly freezing and deglycing, freezing and deglycing all over the world, wherever your frozen reserves are.

Then, of course, the frozen storage.

Luckily, we had freezers in place. We have freezers in place, but we do have to replace those every five, six, seven years because they do run ultra cold. So we look at about $32 million for us just to maintain 68,000 every ten years.

In addition to that, you've got testing costs. We just did a real quick estimate. We looked at six new tests that were implemented since 1991, and so we figured there may be--we assumed that there was probably going to be four new tests over the next ten years. We estimated those tests to be about $25 a test, even though under IND the cost is a lot less, but about $25 a test is a rough estimate. So we looked at $100 a unit to do four additional tests over the next seven years. So that's another $7 million.

Other considerations to look at when you're doing this is that the military has been approved for--and I'm not sure if civilian agencies do this also, but the military has been rejuvenating and been licensed to rejuvenate red cells. In the three to five days post-expiration,

we would routinely add the rejuve-sol, go through the rejuvenation procedure, and then we refreeze them, and those units had as good or better post-transfusion survival in 2,3-DPG as a fresh unit.

The problem with the rejuvenation program and why we put a halt to that until we went through some of these stages was that the specimens, of course, when we were rejuvenating, had been sitting in the refrigerator for 30 days, and they didn't meet the requirements for HIV-1 antigen, which is, you know, the specimen has to be only stored for like seven days or frozen. So we had a lot of rejuvenated units out there that we could not go back and retrospectively test. But we are going to readdress the rejuvenation program, and we may just have to freeze specimens up front in PPT tubes. And then if we freeze those units, then we would have a specimen available.

The other thing to consider is your ABO/Rh mix. We have just routinely frozen all Os just because it's the universal donor. But you don't necessarily have to. If you're going to be setting

up a frozen reserve in hospitals, you could have other Group Os--I mean other groups, As and Bs. It doesn't have to be all Os. But it is something to consider.

That's really the main issues to get across. Right now the frozen blood program with us is on hold until we can resolve these other regulatory issues of the minus 65 degree storage, the shelf life, and the anticoagulant with the FDA, so we're going to be working with them to try and resolve some of these things so that we can get our program moving and going to replace the units that are out there.

We don't want to continue to freeze under our old methodology. We want to use the new methodology and be able to get 14 days.

Any questions? Yes, ma'am?

DR. LOPES: I'm wondering whether or not it's feasible or allowable for you, rather than to destroy outdated units--and I understand why the rotation system may not work for you, but could those units be rotated into the civilian system?

It seems that 85 bucks a unit would be a very small price to pay for the civilian system in areas of shortage to be able to thaw and use those units?

COMMANDER BARTLEY: Well, that's possible, except that we're not throwing them away. The military has decided that even though the license is ten years, we have data that shows that they're good for 16 to 20 years. And so just for military contingencies, for emergencies only, we want to replace these units. We want to have them meet the FDA standards. But until we can get all this replacement going, we are holding on to those units in their quarantine status just in case we--most of them are in, you know, Korea and those kind of places. So we really have not thrown them away.

Now, over the years, we have gone down from the 225 to 65, so I guess that's something to consider. You add in the shipping costs and those kinds of things, too.

DR. BRECHER: Commander, how have you addressed the changing donor qualifications? For example, were you in England for a fixed amount of

time? Have you just ignored those?

COMMANDER BARTLEY: Well, we haven't--you mean for the frozen?

DR. BRECHER: For the older units.

COMMANDER BARTLEY: They don't meet that CJD requirement.

DR. BRECHER: Harvey?

DR. KLEIN: Harvey Klein, NIH. I know you've looked at the cost of this very closely, but I still don't quite understand why you couldn't rotate if these were being put into either civilian use or into military hospitals--in addition to which, it seems to me extremely important that you do continue to freeze and thaw all the time, just to maintain competency of your staff.

COMMANDER BARTLEY: Yes, and we do that within our facilities. We use them for the O-negs and the O-pos to supplement our inventory. So that keeps our competency up. On the ships in the remote areas, they'll go through and do QC once a month and make sure they do their competency. And we try and use them as much as we can, but it's

just--you know, with 225,000 units, it's kind of hard to use all of them. So maybe now that our inventory is down a little bit, it might be a little bit easier to rotate. But, I mean, it's certainly a consideration.

DR. KLEIN: And with 14-day storage or rejuvenation, you're not going to be shipping frozen anymore.

COMMANDER BARTLEY: Right.

DR. KLEIN: You could certainly ship in liquid form.

COMMANDER BARTLEY: Right, exactly. Before, those units had to be used where they were deglyced. And they might not have been needed here. They might have been needed over here. But you're right, with the 14-day post-thaw, that gives you a lot more flexibility to ship products around the country.

Any other questions?

DR. SANDLER: When the Pentagon was hit, Baltimore Red Cross sent 500 units of Group O into the area, which gives you a number, gives you an

idea of what you'd need. If you got an order somewhere, just release fresh blood, we need 500 units of frozen blood prepared, how long is it going to take to start from the freezer and deliver an order of blood on the order of magnitude that's needed? How long for 100 units?

COMMANDER BARTLEY: It's hard for me to tell you right now how long that would take, but it would take a long time. But why would you want to prepare frozen units? I'm not sure the direction you're looking at.

DR. SANDLER: I'm envisioning this as a back-up, I guess. I thought this was a military program to provide blood in an emergency situation.

COMMANDER BARTLEY: We deglyce frozen blood in an emergency.

DR. SANDLER: Is that not one of the options here?

COMMANDER BARTLEY: I'm sorry, I'm not following what you're saying.

DR. SANDLER: If you needed to prepare a lot of blood from this, do you have any idea how

long it would take to prepare it?

COMMANDER BARTLEY: Frozen?

DR. SANDLER: Thawed.

COMMANDER BARTLEY: Oh, thawed.

DR. SANDLER: Thawed.

COMMANDER BARTLEY: Well, it depends on how many machines you have. Like I said, it's one unit per hour. Well, we don't have--most of our machines are in frozen blood product depots around the world. So the medial treatment facilities and hospitals in the United States, there might be two or three in different hospitals. So machines are not available really in CONUS to do this, if that's what you're looking for. They're mostly deployed elsewhere, not in the MTS.

COLONEL SYLVESTER: This is Lieutenant Colonel Sylvester. One thing I'd like to throw in, when there was--it has been used in emergency situations. There was an airliner crash, and it was Okinawa, I believe. And what they did was they brought in the team and they started deglycing and were able to provide. But it's still the limiting

factor one unit per machine per hour, so it's going to depend on which place you're at. Fortunately, at Okinawa, they happen to have 30 units, so they can put out 30 units per hour. So that's always going to be your limiting factor, is the machines.

DR. BRECHER: So we can backfill to replenish the civilian supply in Okinawa, but not in the United States. Is that a fair statement?

LIEUTENANT COLONEL SYLVESTER: We are starting to freeze now at our ASWAs, which we did not do before. Before, frozen blood was all dispersed throughout the world. Now we are starting to freeze at the ASWAs at Maguire, New Jersey, and in California.

The problem you have with moving frozen blood around is every time you move it, you lose some more because it is very, very fragile at those cold storage temperatures. But we are starting to store some here in the United States just to eliminate--we're going to freeze at the ASWAs to eliminate that one shipment step of a frozen product, so let's ship a liquid product to the

ASWAs, freeze there, and then it's ready to go and be deglyced at that point. But until we get the licensure issues overcome, those two frozen depots at Maguire and Travis Air Force Base in California are not available.

DR. HEATON: Andrew Heaton, Chiron. In my experience, the biggest limiter in the use of thawed deglycerized red cells is the post-thaw storage shelf life period.

COMMANDER BARTLEY: Absolutely.

DR. HEATON: And I would very much encourage you to complete the studies to use the old 800-ml Volare bag. The sterile docking technology and the storage solution would easily allow you to get the 14 days.

There's also very good data from Dr. Volare's lab about 20- to 30-year-old storage of additive units, and I believe that you could with an appropriate regulatory program recover the bulk of those units and get the 42-day storage if you design the trial to achieve that.

COMMANDER BARTLEY: Right.

DR. BRECHER: I think it's interesting to hear--and I'd be curious what Jay has to say about this. It seems like you're picking and choosing which FDA requirements you're choosing to adhere to. On the one hand, you're ignoring the European exclusions that the FDA has said we have to do. But you're waiting for approval for 14 days per AS-1, 3, and 5.

COMMANDER BARTLEY: No, we're not waiting. We have an inventory. We're going to keep that inventory until we can replace it. But we don't want to start freezing--we don't want to continue freezing by the old methodology where we only have a 24-hour outdate. We want to freeze to replace these units that has a 14-day, and in order to do that, we have to resolve the regulatory issues before we can proceed with the new methodology.

But we're keeping our units around because that's all we have. If something happens in Korea, that's all we have for 10 days.

DR. BRECHER: I imagine in times of conflict, even the 24-hour outdate on frozen blood,

if that's all you have, you're going to extend beyond that, too, I would imagine.

COMMANDER BARTLEY: We've talked with them about getting a waiver for that.

DR. HEATON: Is it not true that many of your units that you collected antedated the BSE epidemic in the U.K. and, therefore, those regulations would not be applicable?

COMMANDER BARTLEY: Well, I guess some of the units that would be the case, but a lot--you know, most of them were frozen from '87 to '95 time frame.

DR. BRECHER: Jay?

DR. EPSTEIN: Well, from a strictly legal point of view, DOD complies voluntarily with FDA regulation because it's a sister government agency. But the fact is that DOD makes every effort to meet current standards because that's the expectation of the public, including, you know, the military. And there are some difficult situations where the frozen units don't meet all current standards.

Now, we have had different answers in

different circumstances. For example, for P24, DOD made every effort to test samples that were available, and where they were not available, we did permit labeling of units as "antigen untested."

COMMANDER BARTLEY: Right.

DR. EPSTEIN: So, you know, then you get into issues of, you know, is the recipient or their physician informed. So there have been different approaches to the different problems, and I think the bottom line is that it's a disquieting situation until it gets resolved. And, you know, one possible resolution ultimately is to turn over the inventory, and another possible solution is for certain low-risk circumstances to provide variances.

COMMANDER BARTLEY: Right. And, remember, again, that these units that we're talking about that may not meet the current--they're for emergency use. Just like your rare units are labeled in the same way for emergency use. So that's the auspices under which we're maintaining these units. And as we mentioned, we're making

every effort to get those units replaced and to set something up so that we can probably rotate them in peacetime to prevent this from happening.

DR. BRECHER: Harvey?

DR. KLEIN: Harvey Klein. I'd just like to make the same comment that I made to Dr. Gilcher, and that is, in terms of new history type of donor qualifications, the military has the unparalleled capability of tracking its donor.

COMMANDER BARTLEY: Absolutely.

DR. KLEIN: Probably since World War II, maybe even before, so that certainly you could find out that kind of information if your system is set up to do it, exclude those units you want to exclude and keep the ones that still qualify.

COMMANDER BARTLEY: Actually, Dr. Klein, I think we have probably a bigger challenge than Dr. Gilcher does because our population moves around, and then our population gets out and settles down in your area. So the easier way of doing that is if you are in an area where your donor population is stable and they come in repeatedly. Ours moves

constantly.

DR. KLEIN: I know that's true, but as a retired uniformed service, I know they keep track of me all the time.

[Laughter.]

DR. KLEIN: I get mailings no matter where I am.

CAPTAIN McMURTRY: As well they should.

[Laughter.]

COMMANDER BARTLEY: We are working on a single database for our defense blood standard system. When we get that, then we'll have that capability. But until then, right now I have 84 databases out there that don't talk to each other, and so that's a challenge we have to overcome. But we're working towards that.

DR. KLEIN: That is a challenge, but I think that is precisely the issue.

COMMANDER BARTLEY: Any other questions?

[No response.]

COMMANDER BARTLEY: Thank you.

DR. BRECHER: Thank you, Commander.

I imagine all those alumni solicitations also keep track of you, Harvey. They manage to do that.

All right. We are going to move on to a discussion of the AABB Interorganizational Task Force on Bioterrorism. Karen Lipton from AABB.

MS. LIPTON: I can go ahead and start without the slides. Go ahead.

I wanted to let you know actually as I'm speaking here today, I'm really not giving an official recommendation from the Interorganizational Task Force. For all the reasons that you've heard discussed this morning, we don't have a recommendation at this point. But I did want to share with you some of the thinking of the Committee and particularly the subgroup that was put together to look at this issue.

When we first reported out to this group--I think it was almost a year ago--our conclusion was that we couldn't imagine a scenario, a medical scenario where we would really find that we were in a situation where we had increased demand for red

cells that we couldn't really accommodate. And, in fact, our experience after September 11th taught us that we can really gear up for almost three times what we normally collect in an emergency situation. So there is some elasticity.

I think our thinking has evolved somewhat over the last year as we've gone through a number of situations, particularly the HHS, what they call the Top Off 2 exercise, which was a modeled sort of disaster, series of disasters, and then also our most recent experience with the power outages.

In any event, one of the things we found was that what we're really dealing with in many situations is disruption of supply, and that can be caused--I think Ron very effectively pointed out--both by the fact that you suddenly have donors that are not suitable and you have in some situations a moving target. And then in the situation with the power outages, we found some very unusual circumstances in Detroit and in Cleveland where it turns out that their power supply wasn't really based on gravity but was instead based on

electricity, which meant that their water--they had no water. And you might think, well, you can get by with no water, but if you're talking about a facility where you need restrooms and you really do need drinking water for your staff, we found that that was actually potentially a more serious disruption than we thought.

So, for that reason, I think the subgroup that was put together really felt that we would be looking at a number of different scenarios and trying to come up with a recommendation for the task force.

One of the first situations that we actually started looking at when we focused on a reserve was what was really going to be the purpose of the reserve. And, clearly, when we talked about disaster, acts of terrorism, again, it was not so much to focus on increased demand. It was really to focus on the use of a reserve when you're trying to deal with donor suitability and decreased supply related to having to move things around the country when various operations were shut down or when

donors could no longer be--we couldn't use our donors.

One of the things that is up there that you can't see--but I'm sure we will soon--

[Laughter.]

CAPTAIN McMURTRY: You hope we will soon.

MS. LIPTON: Hopefully we will soon. I can tap dance a little longer. There's a comment there about military need, and I will tell you that although we have had previously some preliminary discussions, we're not basing this totally on military needs. The military at this point I think is relatively self-sufficient.

Our concern from a military perspective is our ability in the civilian blood supply to respond to the contracts we have with the military, particularly when we get into situations where we may have two types of issues going on. It's very possible that we could have a conflict or engagement when they're asking us to bring in our supplies, and what we're finding is that we're suffering from some sort of issue in the United

States that will require us to dig deeply into our reserves.

I'm afraid to touch anything. Okay. Let's see. Sorry.

So one of the things we first started to do when we looked at this is to define what we would call the reserve characteristics. And very, very quickly, the group focused on really looking at a very narrow window in which products would be available to ship, and we really talked about four to six hours.

Again, we did this because our experiences taught us that we can go out and increase our collections over a series of days, so the system can respond fairly quickly. It's really if we had immediate needs. So we limited it to looking at four to six hours. We had a relatively amusing discussion, I think, about how many units are needed. You'll see up there we've put a model together on 10,000 units, and you're going to ask us, Well, how did we come up with that? Well, we couldn't come up with a number, and so we almost

backed into the number by saying what could we possibly manage, and we came up with 10,000 in that way.

The other thing we talked about in terms of the reserve characteristics were component types. And by that we really thought should we be focusing on red cells. We did, Jay, in fact, talk about platelet reserves but decided, again, that that was just a little too difficult to deal with and came to the same conclusion that Ron did, which is the platelet reserve should really be in the donor and it would be more effective to have a list of donors that we could call across the country rather than trying to physically create a platelet reserve.

We also talked about what types of units, and we really decided to focus mostly on Os because they really were the most universal and it would require the least amount of inventory.

The final question was kind of an interesting one. We said, Should that reserve be liquid, frozen, or a combination of both? And

ultimately this group decided to focus on the liquid model, and I think after all the presentation you've heard about the logistics and issues surrounding frozen, I think you can understand why we decided to focus on that.

If you think about, I think, with some of the issues particularly that Ron brought up, which is you really can probably use a frozen reserve; but if you think of your liquid as being really your emergency reserve and then use your frozen in a different way, it's probably a better way to look at it than relying on your frozen for your emergency reserve.

Okay. Then we focused on a very, very difficult issue. One is we called it the virtual versus the real reserve. There are many people who believe that we really do have a capability, and if we just maintain extra reserves in the blood centers, when we need them we can call them up. And there are some real advantages of that if you think about it because you don't have to create any separate storage facilities, you don't have to put

personnel into a specific location. It's definitely a lower cost. And then actually trying to maintain those reserves on the local level can end up benefiting your local supply.

Now, at the same time, I think that there is a serious discussion about the disadvantages of a virtual reserve, and there really was a feeling that it would be very difficult to discipline yourself to collect those extra units and not use them. The other concern was that in times of emergency situation, really community blood centers--it would really be incumbent upon them to serve their communities first. And so there was a feeling that a virtual reserve was only that, virtual, and we could get into a situation where we really didn't have access to the units that we needed. The units wouldn't be on site, and there was a great concern over the availability for timely shipment, that if you're trying to collect a few units from a lot of places, there really is a tremendous logistics issue to deal with.

So once we got past those discussions, we

really got into the hard discussion. Well, okay, if we're really going to construct this, how do we put something like this together? We focused a lot on where such a reserve would be housed, and one of the things that we decided right away was that it shouldn't be a single site and it shouldn't be a lot of sites, that perhaps two to three sites that are geographically located on the coast and maybe one in the center would be the best. We also decided that they clearly needed to be located near major transportation hubs.

We talked about who would staff and manage operations at these selected locations, and there was some feeling that these really should be, if you will, some independent entities that would be responsible for managing supply. We did go so far as to talk to some experts who have worked with the CDC on some of their depots and talked about how they managed those depots and got a sense of what it would cost us to set up something like that.

Then we talked a lot about rotation, because what we focused on in a liquid reserve, the

concept is that you would ship units into this reserve, and they'd have to be rotated out routinely. So we'd have to set a number of units that we'd ship in and rotate out daily. We sort of came up with 500 as being the amount that you would have to rotate out on a daily basis.

That led us into some very difficult discussions because to simplify this process we didn't want to be in a situation where we were shipping out one unit to 500 different places. And we realized in this discussion that to really manage this in an effective way, you really would have to be dealing with some fairly large players and large blood centers, which you can imagine creates a political situation when you really have put together a system that is best accommodated by large centers and not by small centers.

Then we talked a lot about the incentives to supply and purchase from the reserve, and I think one of the things we've all struggled with was how would you encourage a blood center to want to participate in this. And we realized what we

would have to do is to set a purchase price. You'd have to have the facility actually purchase blood. It would have to be set at a price that would make it worthwhile for a blood center to collect these units. And then you'd have to have a sale price when the units were being rotated out.

In our initial discussions, we believed that you'd have to set the sale price high enough so that you didn't have local centers that are always having chronic shortages that they didn't start to rely on this. So it had to be set high enough that they would not find this financially advantageous. At the other end, though, you had to set it at a price where people would actually be willing to purchase it. So there was a lot of discussion about incentives and motivation.

Another very sticky question was who could access the reserve and when; that is, who decides when a sale can be made. And we distinguished two situations. We thought there would be a normal sale price from the reserve if people wanted to tap into this. Again, it would not be a particularly

economic price so people would not really be relying on it. But we decided that that maybe perhaps wasn't fair in situations where there was a true emergency, and so that we would set--we thought it would be advisable to set a different price when you're dealing with an emergency situation and that there would have to be a group of individuals or some organization to decide when there really was a crisis.

Now, the task force does this all the time right now, and I think the task force actually would be relatively well situated, since it has representatives from all the national blood organizations, FDA, and CDC, to decide when there really was an emergency that would allow a center to come in or a region to come in and tap into the reserve.

The issue of cost actually was quite difficult to pin down because there are some initial costs in setting it up and then there were the maintenance costs. And if you think about it, they can simply be broken down into the following

categories: You really have to have an initial one-time national appeal for donations to get people to gear up, and I think it needs to be a very public situation. And then if the reserve actually came down below a certain level, you'd have to go out on periodic appeals to make sure that you kept your levels up.

We thought it would be very important to make sure that the public did understand that there was such a reserve and that people would be donating to support that reserve.

One of the biggest costs, though, that comes into this, if you're creating an actual versus a virtual reserve, are the transportation costs of shipping blood to another location and then shipping it out. And all you're doing is adding an additional cost that's related to absolutely nothing except preparing for an emergency. So that is, I think, a difficult issue.

The start-up costs for the storage facility, you really would have to build a facility. There are a number of possibilities, and

what we're really talking about is refrigeration, and then we talked about what it would take to man a facility 24/7. It really isn't that onerous, but it does require some thought and potentially I really think identification of locations.

Ongoing maintenance of the reserve, supplies, power, et cetera, actually wasn't that huge. Again, it was the transportation costs that were most significant. Retention and training of personnel, purchase of the initial units from the blood centers, and perhaps most important, the costs related to outdating product.

We talked a lot about this because, in addition to transportation costs, you're really building in a system that potentially could increase the number of outdates in this country. And right now our outdates are very, very low, so you would almost have to have some sort of public acceptance of the fact that we're deliberately creating reserve and we might end up outdating more units just so that we can be prepared. And it's a tricky issue, but I think it's something we'd all

have to face.

I do think, though, that as people talked about this outdating issue, they thought with 10,000 units that it wouldn't increase outdating very much if we were pretty good at rotating supplies in and out.

We talked a little bit more about national media appeals, the need for public buy-in for this so the donors understood that they would potentially be donating for this reserve. Again, understanding that units would be rotated out of this reserve to meet different localities' needs; that is, even if you donated for the reserve, your unit might get used in a totally different city that wasn't having an emergency, and that also, again, the issue of increased outdates would be a problem.

And the bottom line in all this is that we thought, you know, this really is adding an additional cost, and we didn't think that it was realistic to believe that this is something that would happen unless we were going to get Federal

support, that it really would have to be identified as a Federal priority for the civilian blood organizations to come together and do this.

We said, you know, if we're going to do this, we would need HHS funding as part of the emergency public health preparedness, and that would be funding for the start-up costs, the ongoing operational costs, and then the costs of any of the national media appeals, both the initial campaign and the periodic appeals.

The other thing that I need to point out here--and I alluded to some of the issues that came up in our discussion--we really do need the support of the blood organizations. This is a very different way of looking at a reserve, and it would not work unless people understood that really this was something that really only the bigger centers could participate in; that it would be important, though, for those centers to take this on as a responsibility; and also I guess that the task force would have a role in this.

So, again, you know, I wish I could give

you a recommendation coming out of this group. I think all we did was sort of identify the issues. I will tell you that we did have a task force call yesterday, and we're going to continue to work on refining this model and bringing it forward to the entire task force to look at it and see if there is a recommendation coming out of this. I think it's a very difficult issue for everyone to face, and maybe in the end it is a combination really more of frozen and liquid reserves together. But I think I could represent that it was the thinking of this group that there may be a role for liquid reserves in this, although it was our last choice as we first began our deliberations.

Any questions?

DR. BRECHER: Harvey?

DR. KLEIN: Karen, did your task force entertain the alternate strategy, similar to what we heard from Ron Gilcher, that instead of two or three sites you had 16 or 20 sites, each of which would have a frozen reserve but would be rotating it into the liquid reserve? Because, in point of

fact, what we've heard in the past is that when you need blood, it's the liquid blood on the shelf which is so much easier to ship. Since most of these sites with an enormous amount of transportation capability are also large cities which need blood, there would probably be very little problem with putting that frozen blood into the liquid supply to rotate stocks.

It would, obviously, raise the cost of blood somewhat, but, you know, when you're in a hospital that has generators and probably you don't use them while you're in the hospital, but it's nice to know that they're there in case there's a blackout, so this would be something, it seems to me, that the American public would easily understand.

In terms of start-up, perhaps there is a role for the Federal Government in terms of capitalization. But as you pointed out, the ongoing costs really are quite small, and the ability to continue to keep competency in freezing and deglycerolization is probably very important.

MS. LIPTON: Right. We did look a lot at the frozen, and the reason we quickly turned away from that I think was because of our experience of the past year just in terms of all the requirements that are changing in terms of donor screening and just feeling that it would be so difficult to keep on top of those. But, again, I can't tell you that when this Committee gets back together that they wouldn't be looking at a combination role, again, of frozen reserves and liquid.

And we did talk a lot about having more locations, trying 16 locations. The logistics get to be very difficult with the 16 as to who has what, and that was more the concern, that the simplest way to do it was to just have two depots where you had 5,000 units in each.

DR. KLEIN: If they're all Os and there were 2,000 in each of 16 cities, you'd have an enormous amount of blood, even if there were 1,000.

MS. LIPTON: Right.

DR. KLEIN: And certainly people would know where they were, and in terms of shipping the

liquid blood to any emergency, it would be easier, it seems to me. But that's just an uninformed--

MS. LIPTON: And, again, we didn't specifically talk about 16, but I don't--all I'm telling you is we don't really have a recommendation now, so we could go back and look at a lot of different models. The difficult things becomes--people can't seem to visualize this without getting down to identifying the specific centers, and that always gets to be a little sticky.

DR. BRECHER: Lola?

DR. LOPES: I think that the political may be as important as the logistical in terms of the number of centers that I know because the state I live in is one where we have a lot of communities that are in the western region, very small communities, underserved from their point of view by our universities, which are all in the eastern part. People who feel that they're underserved and are being dissed by the big cities contribute to the environment in which no one is willing to have

taxes pay for anything useful.

MS. LIPTON: That's a very good point.

DR. LOPES: And I think that that's something that really has to--there has to be Federal support for this, and that's going to need to involve all of the communities saying we're part of this.

MS. LIPTON: I think that's a very good point.

DR. HEATON: Karen, as a practical matter, when one runs a blood center, it's very hard to divert significant quantities of Group O into strategic reserves. I was involved in the initial DOD program to prepare the strategic reserve, and I remember just how difficult that was.

So I would urge your group to consider both a combination of liquid and frozen because the reality is there's a constant low level of Group O and you can rejuvenate it, and with the appropriate freezing and thawing technologies, and assuming the appropriate studies are done, you can, in fact, run a low-level turnover just driven off your outdates

Os if you had access to the rejuvenation technologies.

But don't underestimate how hard it is to divert those initial Os to get this started. It's very, very difficult indeed.

MS. LIPTON: Yes, and that was a large part of the discussion about how you would actually--you'd really have to have this national media campaign, and you'd have to make it--I really think emergency preparedness from the highest levels of our government as saying it's important to do this. But I will take that recommendation back to the subgroup.

DR. GILCHER: Karen, there are two things that really in a sense turn on Oklahomans to donate. One is civilian crisis and the other is military crisis, or at least the perception thereof. And I think that's probably true in the whole country. But when people were trying to incorporate that into our model here of getting people to donate, that is, the Group Os in the system that I presented earlier--and we think we

can do that. We think that people will donate, that is, the Group Os will donate knowing that they would be supporting potentially civilian crisis but also military crisis, because we have so many military locations in Oklahoma and a lot of military retired and, you know, dependents. So we get tremendous support from active military and from retired military.

MS. LIPTON: I think, you know, we have not had discussions with the military about this. They are part of the task force. But I think if we get up to a certain level, you know, we would talk to them about trying to make a combination reserve. I think it makes more sense from all of our perspectives.

DR. BRECHER: So, Karen, where are we with the recommendation for two or three strategic sites? Still under discussion? Are you ready to ask for government money or--

MS. LIPTON: No. I think that until the task force really has looked at it and feels they have a plan that they could get implemented,

whether they have the funding or not, I mean, you really do need a certain amount of buy-in, I think, from the blood centers, from people who think they're going to be the blood center that has to go out and collect those Os. So the answer is I don't think we're ready to make any recommendation. We put this as a top priority on our last telephone call, but I still imagine we're months away from a recommendation here of any sort.

DR. BRECHER: Okay. Any other questions or comments? Jay?

DR. EPSTEIN: Well, I feel a need to understand better what drives the need for the frozen reserve. I understood, I thought clearly, from Commander Bartley that was drove the military's thinking was that they were going to have a 72-hour lag time until they could collect fresh blood from a donor, get it screened, and get it shipped. But the issue, it seems to me, from the standpoint of a national reserve is how quickly can you replenish what you need immediately. There seems to be general agreement that the blood you

need immediately needs to be liquid blood on the shelf because nothing else can be done fast enough or in sufficient volume.

So what we're really talking about is what's the strategy to replace what's on the shelf when you suddenly have a surge need for what's on the shelf. And that question devolves to where are you going to get it from and how quickly can you get it to where you need it.

And it seems that the attraction of frozen blood is that the thinking anyway is you can park it where you're likely to need it or be able to transport it quickly, putting aside for the moment that there's sort of a rate-limiting factor in how quickly you can generate the liquid form.

So what it really seems to come down to is what's more practical: having frozen depots that are hard to mobilize or having other strategies to move blood where it may be available from an existing liquid inventory. And I guess I just feel that we need to hear a little bit more about the circumstances that would drive you toward the one

conclusion versus the other.

I think, you know, Karen, you stated that the task force subgroup thought this through and ended up focusing on liquid reserve. But I think what I'm asking is, Well, can we understand the rationale a little bit more clearly? Because as I sort of sort through this, it seems as if the real issue is how quickly can you mobilize blood, and I don't exactly understand what the circumstances are that would lead you to prefer the frozen versus prefer the liquid.

MS. LIPTON: The reason we did come up with liquid was exactly the issue, once you put a time parameter, how fast can you get this many units to--you know, how can you best prepare yourself to be able to ship 5,000 units on four to six hours' notice? And once you come to that solution, you really can't get beyond--okay, you've got to have them in one place. You can't be shipping to one place and then shipping to another. Just physically trying to get the centers all--once you even put out an alarm to everyone saying we

need all these units, the one thing that people who get blood in from other organizations say, it is terrible to get it all in these little packets. What they wanted was, you know, give us everything in one shipment, don't nickel and dime us to death.

And so it really was an ease of logistics that led us to say what we're really talking about is a warehouse or a depot of liquid reserves that could be shipped at a moment's notice to any place. It's just so much simpler in terms of trying to get the blood there in a timely way. That's why we focused on liquid.

DR. EPSTEIN: So is the argument different for DOD?

COLONEL SYLVESTER: When we talk about the 72 hours, our concern is a no-notice contingency. War breaks out today, a contingency breaks out today. We're talking--I can dump my shelves, which is about 700 units, but then I've got a day or two to get them out. And then I've got 72 hours before my donors centers are geared up and producing. And then I've got to ship them. That's another day.

Then they get palletized, and they get shipped to that theater. Well, that's another day, two days, three days, four days, depending on the pipeline they're going through.

So we have to plan for anywhere from seven to ten days where we have to have something out there. Do we want frozen blood? No. But it is the only stopgap measure I have today for a seven- to ten-day gap and getting my liquid pipeline flowing, and so frozen is all there is. And as Commander Bartley showed you, it has a tremendous cost, it has a tremendous logistics burden. Even out in the field it's very difficult to use, but it's all I've got. We're banking that hemoglobin-based oxygen carriers are going to come down the pike and give us a long-term capability to have storage and be able to pre-position those, in which case we can move away from our frozen reserves because we would prefer to do that.

MS. LIPTON: But, Ruth, if you were tied into this system, it is something that the military could access also almost immediately.

COLONEL SYLVESTER: Oh, absolutely. You know, if we knew there was 5,000 units sitting on a coast ready to go out, again, that reduces my requirement for frozen. But even then, to get it where it needs to go, I'm talking about at least a day. And that's where we're hoping hemoglobin-based oxygen carriers come to fruition. But at that, I think we're two to five years away, and so we still have to have something. So we have to replace our frozen stock for all of the other problems that Commander Bartley mentioned.

DR. BRECHER: Jerry?

DR. SANDLER: Karen, I can follow the way that the committee came down on liquid reserves versus frozen reserves. Could you address a little bit more the second decision, which is having gone that way, it seems that there are two ways you could go. One, you could build up the existing infrastructure and say that we're looking at every possible combination and having that reserve everywhere around the country with adequate blood, we could probably on the spot make quick decisions

and get things around, versus--what sounds like a very limiting situation--putting all your money in a couple of banks and hoping that, you know, you could handle it out of that.

Could you explain how you went the bank way as opposed to just building up the infrastructure?

MS. LIPTON: Again, it was really the--if you're going to manage this program, it's much simpler just to have two people in two locations who are doing this rather than trying to coordinate 16 or making those calls to the 16 places. And it just gets more complicated. It's not impossible, but it is clearly easier, you know, if you're going to say I want to mobilize and I want to have this blood available. And if you're talking about military needs, I mean, Ruth sort of hinted at this, that what they need is the blood has to get there, has to get put on the pallets, has to be ready for shipment. So physically getting something there, again, it's a lot easier to go in and collect one thing of 5,000 units than

collecting from all over the place.

DR. BRECHER: Lola?

DR. LOPES: I wanted to ask Ron Gilcher what were the factors that made you go toward the frozen reserve.

DR. GILCHER: The reason we looked at the frozen is because we will have more units in the system. The system isn't a straight line. The system is a sine wave. But, in fact, we can compress that sine wave by being able to feed more of the frozen units in as liquid--14-day-shelf-life liquid units, and at other times we can increase collections. There are going to be times when we can maximize collections and at times we'll need increased usage.

Our concern is also decentralization. I'm concerned if all the eggs are in one basket or two baskets in the country, that becomes a prime target for somebody. They could destroy the system, destroy those reserves pretty easily. I think there is value in decentralization. That is, in fact, part of the reason that we want to move those

2,000 units in two different locations of 1,000 apiece. Also, the value I think of frozen comes down to what if we take out the donor base because of something, and I think that that's one of the additional values of having the frozen red cell over the liquid.

DR. LOPES: So if I'm understanding correctly, you have the big emergency in mind with your concern about the donor base, but you're also trying to, for normal operations, reduce the variability in the system, flatten the sine wave.

DR. GILCHER: Yes, to some degree. We would be using that--as I said, we would be rotating those units, about 700 units per year.

DR. BRECHER: Judy?

MS. ANGELBECK: Judy Angelbeck, Pall. I want to clarify something about donor and appeals to donor based on some comments that Ron made.

Karen, you talked about initializing this with a national appeal, and, Ron, you commented earlier that you felt you'd had one of the most dismal summers with regard to collections because

of donor apathy. So I guess I have a disconnect as to how we would do that. Essentially, the place we begin with all blood products is the donor, and we have--and what I've observed in current years is we have a challenge there with getting more donors to come to the collection.

So a fundamental education or appeal program on a national basis needs to be strong, frequent, and present, even first as a platform to any national appeal to set up a reserve.

DR. GILCHER: There's no question that we have donors--let me say it this way: The good news is this country has more people who are capable of donating at any single point in time than we would ever need. The bad news is that they don't.

But it's very clear in our system, and I'm sure in every other system, we have those donors who respond to crisis. And then they kind of disappear; they don't come back. Or if they perceive that they're donating for a crisis, and this is where we think we could get these donors to come in to donate.

The summer has been dismal, even for us, and that, again, would be the value of having frozen blood because we can build our reserves, and remember again--I want to just stress the point--that the frozen blood is not our emergency reserve. The liquid is. We're really designing our system to use liquid blood, and we could ship the liquid blood, and then we can generate basically 120 Os with six devices per day. We could even do more if we needed to. And they could then be--because they're Os, they can be used anywhere in the system.

MS. LIPTON: And to Ron's point, I think we really thought that if you made public--this program was made public, you really wouldn't have a problem with people wanting to donate for something like this. We've done a lot of donor-focused research because of a joint effort between America's Blood Centers, Red Cross, and AABB in focus groups, and it really comes down to, you know, show me that it makes a difference. And this is something where I think people would think it

really is making a difference because I'm helping to maintain this reserve we might need.

DR. BRECHER: Karen, I wonder. The real question really isn't whether we need a distributed reserve or a centralized reserve, because we've demonstrated in multiple disasters through the years that we have huge surge capacity in the system, and we can meet almost any virtual disaster we could think of. But the day-to-day problems we have are regional shortages, and I don't hear anything about any system that is going to help that other than perhaps if you have a centralized reserve that can then feed into these regionalized shortages.

MS. LIPTON: The purpose of this was not to create a system for regional shortages. That's not what we were looking at. We recognized that this would be very interesting because you could use it. But I think we were a little bit fearful of not keeping that responsibility for maintaining local supplies back in the blood centers that are responsible for that, that we shouldn't be creating

something that--you know, if a blood center is not getting out there and is not successful at recruiting donors, then there's a problem. It shouldn't be just done on the basis of a national reserve. And I don't think that our task force ever thought that our role was donor recruitment. Our role may be messaging to donors and donor education, but recruitment happens at the local center level, to my mind, in the local community.

DR. BRECHER: Harvey?

DR. KLEIN: Again, I don't think that we can model this for the task force around the table today or tomorrow. But going back to the January 2002 meeting that we had here, in the civilian sector it was really hard to come up with a scenario where you would need more than a couple of hundred units of blood. A thousand units is unheard of. I mean, 9/11 didn't need a thousand units of blood. And one of the problems simply was getting it from here to there, especially if you have flights that can't take off and land.

Again, that sort of argues for a

decentralized system with a back-up because obviously liquid blood is what goes first and foremost.

The military system may be a little bit different. In fact, it's probably quite different. But, again, in the past the country has been very able to mobilize from the civilian sector large amounts of liquid blood on almost a moment's notice to supplement what the military has already sent. And the problem, as I understand it, has been backfilling then so that the various large cities primarily can continue their tertiary care responsibilities as that liquid blood is flown away.

So, again, I don't think we can model that for you, but I hope you'll bring those kinds of issues back to the task force to think about. It seems to me that two or three centers with enormous banks may not be the right approach.

MS. LIPTON: Well, actually--you're absolutely right, and I said that. We couldn't envision an increased demand such that we would

need this. What we started to recognize was the concern that if some of these scenarios actually do play out, we may have whole regions that can't collect at all, and that's where we thought you would really be talking about replacing an entire system, not just responding to victims but trying to get enough blood that would replace inventories for blood centers.

DR. KLEIN: And that might in some ways argue for the frozen reserve simply because you need that length of time until your donors might once again qualify, and 42 days simply may not be enough.

MS. LIPTON: You know, I guess as we're talking here, one of the things we can encourage the task force to do is to come up with several different scenarios. And, again, I think that defining the purpose is really very important. What are we trying to accomplish with this? And that's where it kind of gets--again, it gets very difficult. You know, what do we intend this for? And if the Committee would care to give any

guidance to the task force on what we really think we need this for, it would, I think, clarify the thinking in the subgroup.

DR. BRECHER: Okay. Thank you, Karen.

We're going to take a break for lunch. Why don't we take an hour? We'll reconvene at quarter of 1:00. Hopefully we'll get out a little bit early today.

[Whereupon, the meeting was recessed, to reconvene at 12:45 p.m., this same day.]

AFTERNOON SESSION

[12:56 p.m.]

DR. BRECHER: We're going to reconvene. One housekeeping item.

CAPTAIN McMURTRY: I just need the record to show that Dr. Penner is here and Dr. Hoots is here.

DR. BRECHER: Okay. Our next speaker is German Leparc from the Florida Blood Services, and he'll be speaking about management of hospital reserves.

DR. LEPARC: Thank you. I was invited here to present some of the perspectives from the blood center, although we're truly a hybrid entity in the sense that we not only collect blood but also operate transfusion services for about 15 hospitals in our region. We collect about 180,000 units of blood, and two-thirds of them are transfused by our own transfusion services at different hospitals.

That would put the collection level at around--somewhat over 1 percent, and I say somewhat

over 1 percent because I don't think that anybody knows how much blood is collected in the United States. I don't think anybody knows how much blood is there at any given time. And we're talking about blood reserves and what to do, but we'll be making a lot of decisions in the dark because there is no access to real numbers. We have some numbers that are maybe two, three months old. All that blood that we counted has already expired, no longer on the shelf. And I think it's a shame that Wal-Mart can tell you how many cartons of blood and how many egg cartons they have in any super center in the world, and we are not able to tell how many units of life-saving blood we have in our health care system. And what we need is a realtime system, not something that gives you a snapshot of what happened five, six months ago or even a year ago but, rather, if we are going to make decisions and triage blood and have repositories and things like that, I think we need to have also--together with all the other infrastructure of freezers and refrigerators and stuff, we need to have some kind

of information system that gives us access as to where the shortages are, regionally, locally, things that involve more than just blood.

I think we learned from September 11 that reagents can come in short supply, especially when the airlanes are closed. There's no way of moving stuff around. So I think, if anything, we need to expand this issue beyond just the physical repository but, rather, the management systems that are required to make the right decisions so we can send the blood to the right place at the right time.

Having said that as an introduction, some of the things that I will mention will apply not just to the long-term frozen storage but also to liquid inventories. When you're talking about building a reserve, you're putting on--if it's going to be the blood centers that will have to shoulder that or the hospitals will share that responsibility, you're putting on a new task to do to people who are stretched fiscally, stretched operationally, and who, you know, are being

challenged constantly with new projects to do. So we need to take that into account.

The aspects that I have listed there, logistical, regulatory, operational, financial, and ethical, are involved with operation of repositories and particularly with some specific problems that affect long-term frozen storage.

There was an excellent presentation this morning about the Navy's logistics and problems they had to face in managing the long-term frozen inventories they had. You saw the amount of pre-storage processing that has to be done, the storage facilities that they have. I don't think that many of us can afford to have that in every community, and definitely this will have to be a common effort.

There are issues with thawing and distribution, centralized versus decentralized. I'm glad that was discussed because you cannot put all the eggs in one basket when you're talking about disasters. That could be a problem in itself. And back-up systems. You had power

outages, water outages, other things that are part of the essential infrastructure, no phones and so forth, that are needed to support all that.

Part of the logistics also has to do with the availability of proper informatics, keeping an accurate donor record database. Long-term storage may mean having to go back and see who was the donor for this unit, what kind of questions were asked of this donor. We have to have some kind of record, and they may be different in each location because it may vary from region to region what kind of questions are being done. Remember, there is not as yet a uniform donor questionnaire. So, if anything, we have to make uniform is we're going to put blood in a participatory, well, at least all the donors should go through the same screening process and not have a hodgepodge of things.

When you are talking about massive processing of blood, like very complex procedures involving freezing long-term blood, you have to have very accurate cGMP tracking mechanisms. You are using all kinds of solutions, different

manufacturers, lot numbers. You may have bad lots, contaminated lots, all kinds of things. You need to have that capability of going back and tracking everything that may have gone wrong. We live in a very, very regulated environment, and, you know, those of us that do not have the luxury of volunteering to have the FDA come and look at us--but actually they come and look--we have to have all the cGMP things in place.

We have to have very good inventory lookback capabilities. There are mandated steps that we have to take when a donor has a positive test result on a subsequent donation. We have a prior record of donations. Well, we have to go back and within certain periods of time--this is not something when I have time I will do it. Our regs are very specific. Within 72 hours of a positive HIV, you have to go and fish everything out of the inventory.

Well, it is one thing to go to a double-door refrigerator and fish it out of 50 units. Another thing is having, you know, 500 freezers

with thousands of units there and having to get that unit out. So you have to have very good and efficient systems to get these things out.

Bar coding. Bar coding is a logistic problem, and I think it's a problem that can be overcome. But we will need to have a system in place to make sure that no unit in the system has duplicate numbers. Besides being a blood center, we also test for about 14 blood collection agencies in the United States. And I can tell you, the number one problem has been allocation of unit numbers so that you are not testing units with duplicate numbers.

Hospitals have overcome this problem. Many hospitals receive blood from different areas of the country, and they overcome that by renumbering blood. If I have any advice to give people, it is don't do renumbering. I cannot tell you how many times I've gone as an expert witness for legal counsel who had this problem of somebody that was transfused in 1985 and had AIDS, and we're trying to figure out where did this blood come

from. And so, you know, of course, everybody that sent the blood there is part of the lawsuit. And that's beyond the lawsuit problem. It's a question of good tracking. We need to have good bar coding mechanisms.

Now, there is ISBT 128 that presumably has the capability of having no unit on earth that has the same number. We need, again, the regulatory foundation to make sure that we have that system in place that is acceptable.

There may be new technologies that are developed in that place, and we need to have plans for transition. There are many hospitals right now that do not have ISBT 128 capability. So if you're going to send blood that is labeled in a way that they cannot use the bar codes, again, we need to have those things thought out in advance.

Then you have the logistics associated to new technologies, for example, new transmissible disease testing technologies. What are we going to do? Say right now we test for hepatitis B surface antigen by ELISA. It may be that pretty soon we

may do the same test by nucleic acid testing, individual NAT testing for hepatitis B viral genome. What do we do with those units that were tested? They were for hepatitis B, but, you know, with a system or a method that is not current, doesn't meet the safety requirements that we expect.

New marker screening, questions of, well, new disease. If a test comes up for CJD and, you know, you have some units that are not tested for CJD, what are we going to do?

New processing methods, again, the Commander for the Navy showed us the situation where they are where they have units processed under an old system. You have new technology. There is yet a new one, the hollow fiber technique that seems even better. Well, the minute you make that switch, you have whether it is compatible or not. There is a legacy problem there. There is also--regulatorily, you know, we cannot use a positive control from another lot without getting into trouble. I don't see how we're going to do

all the variances that we can do. We freeze under one system and thaw under another system. We'll have to resolve that properly before we go into that.

There was a lot of discussion--and I think it was a very good one--on turnaround time. There are lab demands and instrument demands you have to have, and it takes--there's stuff that you cannot rush up. I always have a discussion with surgeons regarding fresh frozen plasma. They wanted to have it in five minutes, and I said, well, until we can change the law of thermodynamics, you know, we cannot heat up a unit of plasma fast enough. It takes time to thaw a unit of red blood cells, you know, and deglycerolize or treat it to make it fit for transfusion.

I can give you an example. On February 21, 2001--and I remember that date because I had to make a decision of calling all hospitals or sending a message to all hospitals to cancel non-essential surgeries because we had the first such kind of blood shortage in 30 years. And we had been using

our frozen reserve. Of course, we hadn't planned well enough. We had only three machines, and we had been importing blood from the outside. That well dried up. We started processing our own frozen inventory, but with three machines, we could do about 50 units a day, and that wasn't enough to serve just our--one of our hospitals is the fifth largest solid organ transplant center in the country. So definitely we have to have a good turnaround time, you know, commensurate to the needs that we project.

Another thing we found out is that when we rushed these things, people did not follow procedures, took short-cuts, and some of our units did not pass QC. And these are things that you need to have, test the system under stress to make sure that everything is handled safely.

I think we all would agree that at this point the regulatory environment is not adequate for the handling of long-term storage. We will need to plan ahead on the regulatory end how are we going to deal with certain things. Right now we

have the system that was described by the Navy, the 800-ml bag and CPDA-1 blood. But the real world doesn't use those bags. You know, the real world uses different kind of equipment. So we have to make the system compatible with what we use every day. Otherwise, you have compliance problems. You have people handling different bags, more opportunities for errors. You know, are we getting the right people and the right bags and so forth?

How are we going to handle it regulatorily when units don't meet requirements, either donor history, testing, and so forth? I heard Dr. Epstein mention I think we can arrange for variances and stuff, and I think we need to think the process ahead of time. I think it is doable. It's not an impossibility. But it needs to be done ahead of time because we've seen variances issued on 9/11 that later on were rescinded, for example. We had the situation where blood was collected with certain personnel. Then that blood--an urgent variance was given, and then that variance was rescinded, and you had blood that could not be

used. So we don't want to get into that kind of situation.

Then what are we going to do when we have blood in a repository and the agency that collected and processed it now is subject to regulatory action? We need to think of that ahead of time because, you know, I think there is--there may be something that may preclude those units to be used, or it may not. There may be mechanisms to solve that, but we need to think about that ahead of time.

Again, labeling and bar code requirements, we need to have a system that we all can use, that we have regulatory clearance to use, and that is useful in a scenario where you have multiple providers from all over the country.

Operationally, I thought it was very interesting, the dilemma in which the Navy was caught with the situation of testing the aliquots that they had. They were not processed properly to allow for molecular testing. And who knows what the next technology is? Right now, for example,

REDS system had a very good system where they kept not only plasma or serum but also mononuclear cells because there may be technology and maybe there's a new pathogen out there that resides only in mononuclear cells, you know, and that's where we ought to go and look for it, not in the plasma.

Inventory build-up, I think we do have the donors out there if we go with the right message. But, you know, it will be a call to arms, so to speak. Pardon the pun. A call to arms to build the blood reserves. Maybe we can have a system where we can--just like people sign on now, yes, I want to be an organ donor. Well, maybe we can sign them on to be a blood door, to join the blood reserves and give them a number, and then you can say, look, if your number is--your last two digits of your blood reserve number are 10 to 15, come on down tomorrow, you know, so that you don't have all these people coming at the same time, and you can build the reserves that way, and you can put these people to donate once or twice a year.

A rotation of inventory can be done with

proper logistics. Again, you have to have good informatics.

The situation there, we have to be very careful because there's the issue of cost. If we have a rotation of frozen inventory, one example of the quandary we have is leuko-poor blood. At times we have units of blood that the only available compatible unit for that particular patient is leukocyte-reduced by filtration. But neither the physician nor the hospital asks for it, and they tell us: We're not going to pay for the leukoreduction, we just want a unit of blood that is compatible. So if leukoreduction has been done, you'll have to eat the cost. That's what the hospital tells the blood center.

Well, if we have that--I mean, they are stretched to the limit, and they're fighting over every single penny. And we need to have a way to be able to rotate inventory but solve at the same time that demand from the user.

We may have situations where we have to do additional processing of blood. For example, let's

say that the blood needs to be irradiated. Well, there is not such a thing now, a license to have irradiated frozen blood. We have to solve--those things are solvable, but we need to plan ahead. How can we get all these special things done if in the future we license a system to do pathogen inactivation? Well, will we be able to do pathogen inactivation in frozen units? Can we do it or not? Maybe we ought to also think about that. You know, additional processing, we'll have to set it up in a way that allows us to get it done.

Triage in the event of massive needs. If there are several areas, who gets what? You know, we have this centralized system or decentralized system, but who is going to make the decisions of where the blood goes? How does the system get activated? What are the things that would trigger such a type of activation?

Financially, there's a sizable capital investment. I'm not going to go too long over that, but definitely we have to buy places, equipment, computers. Operational costs, who will

pay for that? That needs to be resolved.

Lastly, we have ethical problems, for example, testing for new pathogens without prior consent. Going back to CJD, here's a condition for which there is no treatment. There is no way of avoiding it anymore or a cure. And the donor that donated about five years ago never gave consent to be tested for CJD. Should we? I don't know. That's why there are ethicists that know a lot more than I do, but that needs to be resolved ahead of time.

When we collect blood, there is always a possibility that the donor might die before that unit gets transfused. And I don't think we think much of it. The possibility is probably remote in most cases. But if you have a long-term frozen repository, you may be transfusing blood from dead donors. Now, that may not be a problem. Nobody might think anything about it. Well, this is a legacy this person left. But it creates some problems. There is certainly not going to be any lookback from that. Should we remove units of

blood from inventory when the donor is dead? I don't know.

Then should we use units of blood when the eligibility criteria or testing technologies evolve and cannot be applied to this? There's an ethical--yes, we can do the variances. We can take care of it legally, regulatorily. The question is: Is it the ethical thing to do?

Some people say, well, we can rotate the--if we know that CJD is going to be licensed, well, let's rotate it, use it now so we have all the untested out of the way. I'll just remind you that they tried that in France, and a lot of people went to jail for that. I don't want to make that decision because, you know, I think that maybe land me in jail. So that's a tough one that will need to be solved.

Let me just finish by addressing some issues related to disasters and that have to do also with the reserves. And reserves are more than just the physical reserve of blood. There should be reserves for testing capabilities. During 9/11,

we saw collection jump up five times the normal level that we get every day. New York Blood Center, I am told, had collected record numbers--record numbers--of blood on September 12th--you know, 11th, 12th, 13th. On September 14th, they had no platelets. They were importing platelets from other areas because the testing system was so gummed up that they could not produce a test result before the platelets expired.

So, you know, again, it goes beyond just having enough blood. We need to have systems to deal with upsurges in times of critical response to critical events. That needs to be addressed in some way or another together with the long-term reserve.

I worked there for many years with the chairman of our board who was an executive in a power utility company. And he always reminded me that blood banks are very much like a power utility because you deal with stuff that you cannot store in large amounts. You know, it has to keep moving. And we rendered a critical service to the

community. And I think the power systems, we know how critical they are. Sometimes it breaks down. But they have this system that is constantly monitoring how much voltage is, or amperage, whatever it is that they measure, where to move these things around if the system cuts here and there. And, you know, somebody is minding this whole system, and sure, it will break down and it makes NBC News and all that stuff. But the system by and large works.

What I'm trying again to bring the point to is we don't know how much blood is there. We have anecdotal things. You know, Dr. Gilcher tells me our blood inventory is terrible this summer, and we will all commiserate here and there. But we don't actually know how much blood is there. There are small hospitals that are squirreling blood, having a lot of blood there that they're not going to need, and there are other hospitals that are screaming for it. I think that our country and our citizens deserve a better system. We need to have a good way to monitor our inventories and our

capacities so that we can help each other better and keep the integrity of the health care system through thick and thin.

Thank you very much.

DR. BRECHER: Thank you, Dr. Leparc.

Questions, comments? Harvey?

DR. KLEIN: German, you've obviously given us a lot of thought, and you've had a blood reserve in the past. What kind of a blood reserve do you have now? How do you deal with that issue?

DR. LEPARC: Well, at this point we have a--we learned some lessons from February 2001. We keep about 500, one full freezer with Group O blood, largely O-pos. We never have enough O-neg to put into the system. So it is, I would say, 99 percent Group O-positive blood.

We do have some more extra capability, but right now we can process about 100 units a day of frozen blood, which means in five days we'll be out.

One problem that we see is that there is attrition day by day into the system. You cannot

make up for that, so you eventually get to the bottom of the barrel there, too. So it's good only for the critical time, but long term--you know, it will buy us a little time. Mostly what we use it for is when we go and appeal. If you go and appeal, there is a lag time of 24 to 48 hours before those units come out of the processing system. So it buys us some time when we go and appeal, but it's not practical at this time for us for the scale at which we can apply it.

DR. KLEIN: With some of the technology that we heard about a little bit earlier this morning, do you think that that would impact at all on how you would manage reserves?

DR. LEPARC: Yes. I think if we had the capability of having 14 days after thawing, we would expand our frozen storage, which is the other problem of the short storage time we have after the blood is processed. By the time you get it to the hospital, it's got only 12 hours left, and that is a problem.

DR. BRECHER: Lola?

DR. LOPES: I wanted to ask you and also Jay about how the regulatory system works. Why is it that we have the bags that are currently okay for use are not the ones that are used by everybody? Is it a matter of what gets approved is what gets submitted? Do you have a process, is there a process for moving the regulatory system around to help it catch up to the state of the art?

DR. LEPARC: I think part of it is the data, the process that the manufacturer sends to the FDA, and it's approved for use with that particular bag and their particular system. I think part of the licensing process should be how compatible it is with what we have now, and perhaps if we could, you know, have some kind of legacy requirement or put some incentive for the manufacturer to see that their system is compatible with what is licensed around the country, that would help. You know, that's--probably Dr. Epstein can address that better.

DR. EPSTEIN: I agree with Dr. Leparc's novel products answer. FDA can encourage the

development of novel products that we perceive or the industry perceives are necessary, but we have no authority to mandate that anybody should develop or manufacture them. And when we approve products, we approve them based on whether they're safe and effective, and they're manufactured under good manufacturing practices and that they're labeled truthfully. We're not in a position to pick and choose and say, yeah, but that would be more important. Make that. So we're in a response mode when the companies come in. We evaluate their data. Of course, we may establish approval criteria to set scientific standards, but basically our mode is responsive, whether the demonstration is adequate, you know, has a claim of safety and effectiveness for a specific indicated use been shown or not?

And there are more global issue, and we try to get at those through public fora, workshops, dialogue with the industry, et cetera. But at that level we're simply talking about influence or encouragement. We're not talking about being in

the regulatory mode of requirements.

DR. BRECHER: Celso?

DR. BIANCO: German, very, very thoughtful, very nice again. And you made a very emphatic plea for data and numbers, and I happen to agree with you. I get shocked every Monday morning when I hear exactly how many million dollars a movie made somewhere, but we don't know what we have on the shelves.

But I'm less clear--and maybe you can help--with what we do with those numbers. Let's suppose that Monday morning we had all those numbers. We know in each region, each area, what we have in inventories. What actions could we take? How would we manage these? And most importantly, who would mange this? Would it be Dr. Epstein telling us, "Send blood from Florida to Texas" or the other way around?

DR. LEPARC: I think the last thing I would want is for the FDA to get involved in distributing blood around the country. I don't think that that would be a good way to do it. But

if we have the infrastructure, I think that bodies like the American Association of Blood Banks, ABC, the American Hospital Association, we can have a consortium to operate under certain rules, a system where we all agree we're going to help each other. So you might even have like a board that oversees that activity with patients. I mean I don't see why you shouldn't have the consumers. You should have there everybody that is concerned with that blood, the make sure that it is distributed in a way where it can help the most. And everybody would participate voluntarily into that, but it's got to be I think a multi-effort, just like the bioterrorism task force. You know, we could work on that and we could do it in the private sector with the proper management.

DR. GILCHER: I'd like to also emphasize the importance of being able to track every unit that's in the system. We have the advantage in our system--and hopefully most of you were here to hear my presentation earlier--that we're the sole supplier for the 92 hospitals in our system, so

they're not getting blood from anywhere else. We know where every unit of blood is in our system, but we don't know, at the moment that it's transfused, and we don't know what is on cross-match. We only know that they received the unit.

We've development a software system that has applicability to other systems. It's in the process of being validated now at two hospitals.

I presented some of this data at an earlier Advisory Committee meeting. It was called BUSS, Blood Utilization Software System initially. We've changed the name to Blood Utilization Support System. It's a Windows-based Internet based system, whereby the hospital essentially informs us--it's an online active system--wherever the unit is in their system, essentially if it's been transfused we get data back right away. If it's on cross-match we have data. Now, what we've done to make that valuable to the hospitals is we called it utilization because we put in flags that tell the hospital when they're using a product inappropriately or there's an order that's

inappropriate. An example that I used the last time was if they ordered an irradiated until today, but tomorrow they did not, then one of the two orders is inappropriate. The system flags and tells them that. We don't know which is the appropriate order. But we've done that to try and improve utilization because ultimately that affects the cost, but that will then allow us to truthfully then track every system exactly where it is in the system, and that's the direction that we're heading within our system. But it has the applicability to any system.

DR. BRECHER: Thank you, German.

Our next speaker is Dr. Dennis Goldfinger from Cedars-Sinai Medical Center in LA.

Is Dr. Bowman from CMS in the audience? Okay, thanks.

DR. GOLDFINGER: Thank you.

Actually Captain McMurtry called me on Tuesday and said, "I need a favor. I wonder if you could come and give a talk to the Advisory Committee on Thursday." Fortunately, he picked a

topic about which I know something, so I was able to throw a talk together on Tuesday and he got me a ticket for yesterday morning to fly here. Actually, I have a feeling that he really just wanted the Committee to hear the latest from LaLa-Land without having to distribute tabloid newspapers to the group.

[Laughter.]

DR. GOLDFINGER: What I'd like to do is tell you about frozen red cell applications from my perspective. I've been freezing blood actually for a long time. I started the frozen blood program at the NIH like 33 years ago, and when I got to Los Angeles, I started a program at Cedars-Sinai in the early 1970s. What I'd like to discuss with you is the freezing of ordinary inventory, as we've been discussing this morning, but also give you a little bit of background on some of the ways that we used to use and maybe continue to use a little bit, continue to use frozen red cells, especially at the hospital level with extensively phenotyped units of blood for patients with red cell antibodies and the

freezing of autologous units under a variety of circumstances.

First of all, it's important to remember that frozen red cells were initially used in the past for their clinical value, not really so much for inventory control. Frozen red cells are very much leukocyte poor. 90 percent of the white cells are removed by the freeze-thaw process, and this was one of the early ways for us to supply leukocyte-reduced red cells to patients. Also they're plasma poor. Over 99-1/2 percent of the plasma is removed from a unit of packed red cells by the freeze-thaw washing process, again, making this product useful for patients who have, for example, severe allergic reactions to transfusions. And frozen red cells are the closest thing we have to fresh blood. The survival of these red cells, because of adequate maintenance of ATP levels, is excellent, and their hemoglobin function is equivalent to that of fresh red cells because of preservation of 2,3-DPG.

Now, if we go back though to the use of

frozen red cells for inventory control, first let's take a look at its use for the ordinary control of blood. In other words, freezing away blood when the supply is plentiful, so that it will be available when supplies are short. And from the hospital point of view, I can tell you that this approach used to be a very effective approach. We could actually freeze away several hundred units of Group O blood, O positive and O negative, and at the hospital level, at a hospital like ours where we transfuse 50 to 100 units of blood a day, about half of those would be Group O blood, the ability to pull out 10 or 15 or 20 units of Group O blood every night for availability the following day really did help to boost the supply of blood within our hospital. This used to be the case. I'll tell you why it's not so good any longer. But at any rate, it was an effective technology.

As far as phenotyped units of blood are concerned, this is actually an interesting application. We don't see much of it made use of any longer, but the idea is to have blood available

for patients with red-cell antibodies, not for patients with a single red-cell antibody or patients with an antibody to a high incidence red cell antigen, but for patients who had antibodies, who had multiple antibodies to red cell antigens.

Here's an example of the kind of thing that we used to do. We could have several hundred units of blood frozen away. All the units would be Group O. But we could--looking at the various blood group systems where patients--to which patients could make clinically important, clinically significant antibodies, we could have units of blood, for example, in the Rh system that are R1R1, meaning they're little c-negative and big E-negative, and perhaps this unit would be Duffy-A negative, JKA-negative and Big S-negative. And there's a unit of blood for a patient who has those kinds of antibodies. We might have another R1R1 unit that's Duffy-B negative and JKA-negative. We might have an R2R2 unit, a unit that's Big C-negative and little e-negative, that's Duffy-A negative, JKB-negative and little s-negative.

Having these, you can see that there all kinds of combinations that you could have, and you could have perhaps four units of each and with several hundred units, cover the needs, the immediate blood needs for patients who had multiple red cell antibodies. This is a technique that's just not used very much any longer, but used to be something that was very useful, and made the whole frozen blood concept kind of fly in the path and made people interested in the concept of red cell freezing.

And then finally autologous blood. We've had a lot of experience actually in freezing autologous blood in two ways. One which can still be used, and that is freezing blood for elective surgery. The times that this can be used would be for surgeries where the patient is required, in order to meet his or her total blood needs, is required to put away an awful lot of blood, several units of blood, and especially in the days when we could only store blood for three weeks, this was particularly useful. Now that we can store for

six, it's not so needed any longer, but once in a while is, or for the patient whose elective surgery is canceled and all this blood's been put away, it's possible to freeze the blood.

But also long-term frozen storage of blood. This is something we could store blood for up to 10 years and this is something that became popular in the 1980s following the AIDS epidemic when people became afraid to receive blood from community sources, the idea that they could put away their own blood, and actually, several private enterprises developed whereby patients could, for a charge, put away their own blood for potential future use. We actually started such a program at Cedars-Sinai. Now, I want you to know that I'm not touting this concept. In fact, our own program is largely shut down, really because of lack of interest. And all of the companies that I know that started these programs have all gone out of business.

But just a word about this, because certainly I think frozen autologous blood really

did get a bad rap without data, and we actually have some data. First of all was the cost issue. Well, it's probably not going to be used and it's going to be very expensive. Well, we looked upon this as an insurance policy. And when you buy insurance, if you buy disability insurance, you're not hoping that someone's going to knock your eye out next week so you get a chance to use it. On the other hand, you know that you can't buy fire insurance when your house is burning down. And so you pay the money with the hope that it will never be used, and if the price is reasonable, then this can be considered an okay thing to do. Another issue that was brought up was that--and in fact, what we found in a study that we did over a 20-month period, 21 percent of the units in our freezer, about 1,000 units at the time, 21 percent of those units actually were used by the patients who put them in. So actually, utilization was fairly high. These studies were done in the late 1980s.

Another salvo that was levied against the

autologous frozen blood concept was that it would not be available when the patient needed it. For example, here I am in Washington, D.C.; my blood's frozen in Los Angeles. How am I going to get it? Well, first of all, you probably could get it, but one of the big issues was that you--again, we heard about how long it takes to get blood out of the freezer, but you just never get it to the patient quickly enough. And we looked actually at 1,100 patients prospectively studied over a three-month period, who received transfusion, and found that 48 percent, essentially half the patients, had four or more hours from the time the blood was ordered until it was needed to be transfused. So this blood, if it had been in the freezer, could have met the needs of half the patients who were going to be transfused.

We heard that the quantity would be insufficient. Well, patients would put away some blood, but in fact, when they needed the blood, they get into a car accident, they'll need 20 units, 100 units. What we did is we looked at

4,400 consecutive transfusions of red cells, and found that 78 percent of the patients who were transfused with these red cells used four or less units of blood for their total transfusion needs. Three-quarters of the patients' needs could have been met had their blood been in the freezer. Again, I'm not selling this concept, but the point is that these, these criticisms were really levied without any data whatsoever.

Limited post-thaw storage has always been a problem with frozen red cells or saline washed red cells, and it remains such a problem, although as we've heard, there are some closed systems, the devices that are likely to extend the post-thaw storage.

At any rate, these kinds of programs are unlikely to become more widely utilized. There's just no interest in them and they're not going to have a significant impact in the future, I don't believe.

What about the problems with phenotyped units of blood? Well, the problems here are you

need a lot of storage space if you want several hundred units of blood. The blood is hardly ever used. The cost is not so much an issue when you actually need the blood. It's not such an expensive way to get extensively phenotyped blood, but the cost and the ability to extensively phenotype hundreds or thousands of blood donors, so as to be able to come up with these various combinations of units, is quite a chore, and is something, again, that's not likely to happen in the future, and probably would not happen at the hospital level. If it's going to be useful at all, this is probably the kind of thing that belongs within the community blood center.

And now, finally, what about the problems associated with the ordinary inventory? Well, we've always had some problems. For example, blood has to be frozen within five days of collection if we want to have relatively fresh red cells. There's a problem that hadn't been mentioned earlier, namely, that sickle-trait blood, blood from donors who have sickle trait will not thaw

properly unless you know about it ahead of time. So there could be this problem of having a segment of the blood that would be difficult to get out of the freezer.

But the problem with the frozen blood to support the inventory has never been getting the blood into the freezer. That's really the simplest part of it. You can always come up with enough blood and get the people to put the blood in. And as you've heard this morning, some people who are doing this sort of thing have recognized they need lots of freezers and that's always been recognized and it's something that's not really a limiting problem. It's getting the blood out of the freezer that's the big problem, as you've heard this morning and this afternoon again from Dr. Leparc. You've heard it several times now.

It's interesting to note that certainly several, especially the Department of Defense, has recognized that you need to have a lot of instruments. The cell washing instruments, that you need for deglycerolization. You need to have

lots of these. It's not just that you need lots of freezers, you need lots of cell washers. So in order to get blood out in quantity in a short period of time, it requires having perhaps 40 or 50 of these cell washers in order to deliver this.

But a bigger problem, more trouble, is the staff. How are you going to get staff? If you contemplate that one technologist of technician could operate two pieces of equipment or even three, you're going to need perhaps 20 individuals who are going to be trained to do this. But furthermore, not only do they need to be trained, but those people are going to be sitting around doing nothing for five years, until the time comes that you're going to actually need them to get blood out of the freezer in a hurry if you need in five years, because in fact, in the history of transfusion medicine, we've never recognized a time when we've needed to get all this blood out in a hurry where we'd need these frozen resources.

So I see the problem with adequate staff to be one of the greatest, and really making this

not a tenable approach for the emergency availability of blood.

Now, I'm glad to see that some specialty of the Department of Defense has recognized that the initial response to a disaster has got to be with liquid-stored blood on the shelves, and that these units could then be brought back into the system to help refill the system, and I think that that is an important recognition.

The big problem--and you've heard this now from several speakers--is that involved with the development first of all of new blood tests. This began with the HIV epidemic in the early 1980s. When we instituted a test for HIV in March of 1985, we suddenly had to take all the blood in our freezer and throw it in the garbage. All the blood goes out. Five years later when hepatitis C testing came along, all the blood had to be discarded. None of that blood could possibly be used. And as you know, since then we've continued to add many new tests, NAT testing, now West Nile virus testing.

And so that blood is untested, so we got very bright--as you've heard, other people are bright also even on the other coast--and so the idea of freezing a sample tube, but I've listed it here, and several have mentioned it, that sometimes that sample tube actually is an improper specimen, doesn't even allow you to do the test. But assuming that you could do the test, remember that throwing away all this blood is not just costly, it's demoralizing. When you get your staff to gear up, and if you get the blood donor, the population out there to come in and put away, make this effort to store away a lot of blood at a time when there's going to be adequate supply, and then you throw that blood away, that is absolutely demoralizing, and you can't make up for that, and it's something that's too distressing, to allow you to continue to maintain such a program.

The even bigger problem is that of the new questions. Now, you've heard about some of this discussion this morning, but let me put some additional perspective on this. First of all, this

began with HIV, things like sexual exposure, so we had problems with things like male to male sex or sex with a prostitute. Then we got on to this variant CJD, and we got involved with geographic exposure. Now, more recently with West Nile virus, we deal with signs and symptoms, or maybe with SARS, we deal with signs and symptoms. I believe that you cannot recontact the donors to get this information for two reasons.

First of all, it's just too--it's a logistical nightmare to try and go back and find these donors and ask them these questions. And second of all, they cannot give you truthful--not truthful, but accurate responses to the questions because while they may remember things like where they were, whether they spent a total of three months in the UK over their lifetime or over the period of time for which we exclude, they couldn't necessarily remember particular contacts with high-risk individuals, or having had fever or headache a week prior to the donation that they made two years ago. That's just not possible. And so these units

are inadequate. So that recontacting donors does not allow us, is really impractical and doesn't solve the problem. So we would continue to lose our inventory.

And so, what's my conclusion? I'm sorry to say, I really believe, that frozen blood storage is dead, and this is after over 30 years of trying to make it work in every conceivable situation. And I must say Dr. Leparc actually presented a couple of thoughts that I hadn't even come up with. For example, pathogen inactivation, I hadn't even thought of that one as a reason for again having to discard a freezer full of blood.

I'm really glad to see actually that in Karen's presentation, that her group decided that liquid storage or some other approach to having an emergency inventory availability was preferable to frozen storage because I don't think that we'll ever overcome--I think these are insurmountable stumbling blocks that will not permit long-term frozen storage or even shorter-term frozen storage of large quantities of blood.

While I think that many have made a good faith effort, and once again, I think that the armed forces have certainly done that, and they've clearly come up with some of the answers to certain of these problems, they also recognize, however, that much of the blood in the system will be suboptimal at any given point in time.

Our likelihood of using blood that is suboptimal is really, really small. The fact that the FDA, for example, permitted the collection of all of this blood after September 11th and provided for the possibility for variants, you see, no one ever used any of that blood. Now, granted, it didn't need to be used at that time. But just knowing how physicians and other health care workers, they're going to use this as an absolutely last resort. The idea of pulling a unit out of the freezer when there could be some other way--maybe the blood's going to soon get here from the midwest or something, and if we can just hold out a little bit longer--they're not going to delve into that supply of inadequately tested or improperly

collected for some reason blood.

So my conclusion remains, unfortunately, the same, and I think that we'd all be best off putting our efforts in emergency planning to programs that will be more likely to be successful.

Thank you.

DR. BRECHER: Thank you, Dr. Goldfinger.

Questions, comments? Harvey?

DR. KLEIN: Dennis, I have a comment and a question. The comment is that actually we did have a long-term autologous storage program which you started at NIH. It involved patients who were literally untransfusable, Bombay phenotypes, patients with multiple antibodies. We did publish those data. Dr. Sandler may remember, since he contributed. Almost none of that blood, when it was stored for over 10 years, was used. People disappeared. People forgot that they had their blood in storage. We actually had someone in Washington who went to another hospital, needed to be transfused and found a rare donor across the country, and we had four units in the freezer. So

that blood is rarely used in our experience. That's in Transfusion in 1991.

The question is you seem to focus the presentation on long-term storage, but I'm wondering what you think of the shorter-term strategy that Ron Gilcher presented this morning, where you'd be using that blood and rotating your inventory, so most of these issues with finding the donors really wouldn't pertain.

DR. GOLDFINGER: Yes. And you know, I appreciate these efforts on a lot of thoughtful individual's parts to try and make frozen blood work for them. The problem I see with even that short-term approach is that there's a day on which a particular test is not needed, is not required, and then another day when it is. And even as Dr. Leparc was pointing out, if you kind of know it's coming--and this happened recently with West Nile because we did get some indication that this test was on its way--the idea of kind of like clearing out the inventory, I think in the case of West Nile this would not have been a big problem, because

none of our blood was infected I don't think, and it would have been okay to use up those units as quickly as possible. Plus the units that we were going to transfuse at a particular point in time were not tested either, so I don't have a problem so much with the idea that you're using these untested units. But on the given day that the test is required, any blood in the freezer now is in trouble.

So the ethical issue I don't think is you trying to use up that blood, but the only practical approach then is to empty out the freezer entirely so that you actually have no frozen blood, and now try to refill the freezer with tested units. That approach would work, but that's very difficult to manage.

DR. KLEIN: Dr. Gilcher would have been able to test the specimens that he froze away.

DR. GOLDFINGER: If he has a pilot sample that in fact is adequate. If it's a question, that's a big problem. West Nile is a great example where the question really fails because even if it

was two months ago, to expect that the donor necessarily remembers that he or she had a fever six days before donating or a headache or some such thing, that could be difficult, and so we found--we thought that the testing, which initially threw us for a loop, could be overcome in some way. But it's the questions that have--to me, that's dealt the death blow really to frozen blood.

I don't think anyone here would deny that the kinds of questions that the FDA has asked us to put into place are in fact valid and useful for helping to protect the blood supply.

DR. BRECHER: Celso?

DR. BIANCO: You have challenged us, and now you have to come with alternatives. What is alternative number one, two, three?

DR. GOLDFINGER: I'm going back home tomorrow.

[Laughter.]

DR. GOLDFINGER: These are not easy answer. I'm really glad to see this Committee taking this up, and this is not the first time. I

think as Mark has pointed out, this Committee has brought this to the table going back a year and a half or so ago that I can remember, and I'm glad to see that these are task forces that are made up of the various players in the field. It's very important that we represent the donors in this arena, the patients and such, that I'm glad to see that people are working on it, some pretty bright minds, because I heard some good presentations this morning. I just think that this is a mistake to keep this as one of the possible--again, you may disagree--but to keep this as one of the alternatives, because it prevents us, I think, maybe from going all out in our thinking about how we're going to finally solve this problem because it is a problem that needs solving.

I am convinced even though, for example, with September 11th or an earthquake--we had a big earthquake in California. Let me tell you, that was scary, but hardly anybody was hurt in that one. September 11th, the terrible thing is, that all the people that were hurt, or so many of them were

killed, and so they never needed the blood. But I think we can envision a situation where there would be thousands of injuries, not dead people, thousands of injuries that really would require large quantities of blood. And if that were to happen, and especially if transportation routes were not available to us, as they were not after September 11th, we need a system, I think, but I don't know--it's going to take some additional thought. I think though if we stop considering frozen blood as one of the reasonable options for the majority or at least a significant proportion of that reserve, I think we'd be better off.

DR. BRECHER: Ron?

DR. GILCHER: Actually, I have a question for Dr. Leparc. First let me tell you what we didn't do. On July 1st when we began testing for West Nile virus, we didn't throw out all the blood that we had drawn prior to July 1st, and we did have retention samples. We made the decision not to test those sample, and I'm curious whether your blood center went back and did repository testing.

DR. LEPARC: We did not, but we labeled those units of blood so that when they're released we have to get authorization from the physician.

DR. GILCHER: But the point that I want to make is that I suspect that your center and my center and probably most of the other blood centers, did not do testing backward.

DR. LEPARC: I have to say though that Dennis is right. About a third of the physicians, when you tell them, "Look, we have a unit but it wasn't tested for West Nile and stuff." "Either don't transfuse at all," or they'll say, "Well, can you get one unit," and they will wait for it.

DR. GILCHER: I guess I was more powerful. We didn't have to waste any of the units, but we did have the repository sample, and I think that is an important point, is retention of a pilot sample for testing that can allow you to prepare for a test that's coming along, because none of these test literally are introduced overnight. We know they're coming.

DR. LOPES: It seems that you're saying

that it's not a good idea to take fresh new blood, newly collected, and freeze it at that point within the three to four-day period. For really emergency backup, is it impossible to find ways to freeze blood that's within say a week of being outdated, you know, 35-day-old blood, and let that be what's stored away for really deep emergencies?

DR. GOLDFINGER: It is possible, especially with rejuvenation, as you heard a little bit about, where you add these special solutions that make these things young again. It's the fountain of youth. We don't have it in California, but you do have it in Florida, I think, that fountain of youth.

[Laughter.]

DR. GOLDFINGER: And so we actually could freeze those, but actually, I think it is okay to put away fresh units when there's lots of blood around. There are times when we really have enough blood. That's why I don't think that getting blood into the freezer is the problem, and I would agree, and I think probably the Department of Defense has

felt, that it's better to have some blood that may be just not right up to snuff, but it's pretty darn good, and have that rather than no blood at all. I can't argue with that point. So if there's a place for frozen blood, I think maybe it's that small place. But as I pointed out, and as German has also confirmed, that most physicians won't want to use that blood. They'll use it as an absolutely last resort, but last resorts sometimes come, and maybe in the military that's where they see it the most. I don't have an objection to having that kind of a contingency.

DR. BRECHER: Celso.

DR. BIANCO: I just want to go back to the point that Dr. Gilcher raised. While I don't think that West Nile is a good example, it's seasonal, the risk prior to July 1st is very different from the risk that we have today, just a month later or two months later. So I think that the concern is about diseases that are there the whole time and all that. At least in West Nile we had that difference. And I think that it has to be

emphasized. The danger is another, I don't know, not a virus that appears or even the agent for CJD identified, that we really would have no other way to screen that unit but to go back to the sample and test.

DR. HAAS: Dr. Leparc said that just because of supply capacity he didn't do O-negatives. But if you're going to set this up, say, as your last resort, not to be a major subset but a contingency subset, perhaps regionally or something like that, and you had presumably long periods of time between its use, could you concentrate on just O-negative, just to remove one other variable out of the equation to make availability virtually universal? And then again, you would have to make the decision that you are using it only as a subset of your reserve, I mean as your contingency. Other mechanisms would be your primary contingency, but this would be like your last resort, as you said. Wouldn't that case justify really pushing towards O-neg instead of just O-pos mostly?

DR. GOLDFINGER: Yes, definitely. It can be done, and we've done it. Again, if I come back to--my talk's supposed to really be what do we do at the hospital level. At the hospital lever, where we're not talking about quite such large numbers, but even at the community blood center level, it is definitely possible to put away some O-negative blood, and over time accumulate a fair bit. But I'll tell you, this is one of the most difficult aspects of what I've done with frozen blood, is that I've tried to convince some of my people to do this, to squirrel away whatever extra O-negs could be available, never leaving obviously a patient or the community short of O-negative blood, but put away whatever we possibly could in the freezer, knowing that we can always get it out.

One of the most demoralizing of all issues was that when we finally got to having a substantial number of O-negative units, we had to throw it all out. That was very brutal. So I think it can be done, because there really are times of the year when blood is plentiful. It's

just that there are also times when it's short. I can tell you, two years ago, it was before 9/11, that we saw the worst shortages that I've ever seen in my life, that I never thought I would see, where you could actually walk into a hospital--our hospital is like 1,170 beds--and we had like two units of O-negative blood on the shelf one day. Not only 1,170 and it's a tertiary care hospital, but it's a Level I trauma center, and where you could be dealing with young women of child-bearing age coming in after trauma, two units of O-negative blood. It would be great to have those stocks.

But once again the problem of maintaining those stocks is perhaps insurmountable.

DR. BRECHER: Okay. Thank you.

We'll now move on to Scott Caswell from America's Blood Centers.

Let me make a comment to something Dr. Klein said, that these autologous units that are frozen are not always useful. There certainly are times when there are. When I first came to Chapel Hill we had a trauma patient who had gunshot

wounds. It turned out he had an anti-U. So I said, okay, call the blood center and see if they have any U-negative blood, and the answer came back, "We do," and as a matter of fact there were three autologous U-negative units from him that were right in our region, and it turned out it was the third time he had been shot.

[Laughter.]

DR. BRECHER: The first time he got sensitized. The second time they recognized it and asked him to put away autologous units. And the third time they were useful.

DR. BIANCO: That's the definition of high risk right there.

DR. KLEIN: I think the point, Mark, is that if yo store rare units--and you should, because I think it's a very good idea, and we do--that they'll be there. If you had asked that patient or if you could have asked that patient, he might not have known that his units were stored, might not have remembered, or in fact, you might not have been able to ask him because he might not

have been in the position to tell you. And if his units had been stored at another hospital, for example, you never would have gotten them. That was what we found, and again, we have data on this going back I think 20 years. Some of the units Dennis froze. One of the women was in a nursing home and she had no idea even that she had ever been transfused or donated blood. If she had needed blood, we certainly wouldn't have made the connection.

MS. LIPTON: We're afraid to ask, where is this guy?

DR. BRECHER: He survived. I'm not sure what his current occupation is.

[Laughter.]

DR. BIANCO: Well, you know, this is true even in large systems like the times in New York, with several trauma centers, several hospitals serving populations of thalassemia or sickle cell. And the units may be in one hospital, and the other hospital doesn't know, or the patient will approach a hospital and the antibody will be rediscovered at

that time. It's a challenge.

[Pause.]

DR. BRECHER: We're ready to resume. Take it away.

MR. CASWELL: Mr. Chairman, Committee members, ladies and gentlemen, good afternoon. My name is Scott Caswell. I am the Chief Communications Officer for America's Blood Centers, and my assignment today is to discuss with you strategies to create a donor reserve. I have a couple of comments though at the beginning.

One is I did not bring handouts. I apologize and I will send them to Captain McMurtry, and I have a little bit of a cold, so please bear with me.

Before I get into the presentation I would like to give you the framework from within which our members work each day, and then I'm going to tell you a little bit about who we are.

Current state of blood supplies. When we are asked the question, "How is the blood supply," we usually supply that the blood supply is okay.

It could and should be better, but it could be a lot worse too. Having 76 members complicates our messages as well, and as our colleagues with the American Association of Blood Banks and the American Red Cross can attest, makes joint statements and broad appeals problematic. We have some members who are in dire straits, but ABC has many members who are doing quite well, places like Mississippi Valley Regional Blood Center in Davenport, Oklahoma Blood Institute in Oklahoma, Memorial Blood Centers in Minnesota, are experiencing double digit increases in donors.

So any time we participate in a joint statement or appeal, we hear from our members. Some breathe a sigh of relief and say it's about time someone did something, but others call and ask why we felt it was necessary to go out on appeal. You know, they're fine, and now they need to field media calls asking them why their blood supply is doing poorly and why they felt it was necessary to go out.

But the bottom line is, demand is rising

at a clip of 3 to 5 or 6 percent per year, and supply is barely keeping pace, and in the year 2002 demand actually exceeded supply for our members.

Post-9/11 syndrome. Our reality is the blood supply is more precarious today than it was prior to 9/11. An event that many of us felt would jolt Americans into blood donation, has actually, it seems, had the opposite effect.

Who is America's Blood Centers? I'll be very brief. I would like to remind you of who we are and why we are about our nation's blood supply. America's blood centers is a confederation of 76 member community blood centers, one Canadian-based system, and 75 in the United States. All are nonprofit, governed by an independent board of directors, and licensed by the Food and Drug Administration. Our members collect nearly half of the nation's blood supply, and 25 percent of the Canadian blood supply.

I seem to be experiencing a technical problem here.

I know this Committee continues to discuss

many of the items I will raise in the next few minutes, but again I think it's important to give some context to the discussion.

Mad cow deferrals. It is estimated that Mad Cow deferrals will take more than one million donors out of the system, resulting in a loss of 1.7 million donations. I was in Richmond on Monday at Virginia Blood Services. Virginia Blood Services collects approximately 80,000 red cells each year. This deferral has cost them more than 2,000 donors and 8,000 donations, and while a four to one ratio may seem to be high, VBS has invested heavily in automated collection technology and relies heavily on apheresis donors. The donors they are losing are among their best and most reliable. Not only did they lose donors in raw numbers, but as we all know, repeat donors are safer donors and much cheaper to retain.

The impact of temporary deferrals is much more devastating than one might think. Chances are a blood donor that is temporarily deferred is much less likely to return as a donor regardless of the

reason. When we defer a donor we have probably shamed them, and in many cases told them that they are sick, even though they and their doctor know that they are not. Any donor advocate or recruiter or nurse or physician can give you any number of examples of this from the donors they speak to on a regular basis.

I have some personal experience. I moved here from Minnesota just over a year ago. I had never been deferred from giving blood for high blood pressure. Since moving here my blood pressure seems to have gone from 118 over 68 to 154 over 94.

[Laughter.]

MR. CASWELL: And I would attribute part of that I think to the technician taking the blood pressure because it seems when one person does it, it's higher; when someone else does it, it's lower.

Anyway, the fact is, after I have rearranged my schedule, left work early, braved metro traffic to get to the donor center in my community, and then found out that I'm not eligible

to give, I'm not too happy. And I'm exposed to this every day. And if I wasn't exposed to the challenges every day, I'm not so sure that I would go back and give blood because it's not an easy thing to do sometimes. We don't always make it convenient.

Living in Minnesota, we have a number of folks during the wintertime that like to take warm weather vacations, and we have a lot of folks who go to Ixtapa, Mexico. It's a wonderful place to go. I've been there. But we get people who come back and they say--and they come in to give blood as they regularly do, and then of course, you know, they were deferred. And it's like, "Well, why didn't you tell me I was deferred? Why didn't you tell the news media that this was coming up so I would know? But as we all know, you can't just call the TV station and tell them everything that's going on. But these kinds of deferrals cause problems for blood centers.

Impact of changes to the donor questionnaire. More than one third of our donors

are over the age of 50, and that number is growing rapidly. Many people my age and older do not respond positively to changes in our lives. Repeat and regular donors do not understand why they need to answer the lengthy donor questionnaire every time they donate. Their responses never change. They ask why, if we really were interested in keeping them as donors, why can we not make the process smoother and simpler? Even more frustrating to donors is why we ask additional questions, keep adding them to the donor history? They examine their lives and their behaviors, and they view our questions as an intrusion or as an accusation or as a challenge to their integrity.

I had a 20-gallon whole blood donor remark to me one time that he didn't even understand some of the questions and the behaviors that were implied. They were things he wasn't familiar with. Was he joking? Of course he was. But donors are feeling frustrated, and giving blood, as I said before, is an easy thing to say no to.

80 million boomers are beginning to

retire. 50 percent of the blood is used by people over the age of 65. Clearly people don't need to stop donating blood at a certain age, but life changes are more likely to occur, which might cause a person to stop donating. This situation is very analogous to our Social Security conundrum.

Donor diversity. For the most part, our donors have been very white. We encourage this on the basis of studies that demonstrated the relationships between socioeconomic factors, race and infectious diseases. And I'm not in a position to talk to you about that. You know better than I. But the reality is, the face of America is changing. Look around the room. Who do you see? When I attend a national meeting for America's Blood Centers, or a national meeting for America's Blood Centers, I look around the room and I see a lot of folks who look like me. We need to begin bringing in donors who do not look like us, and we have some significant cultural barriers and decades of mistrust to overcome.

Blood center economics. As you all know,

this is a very complex business. We have a business model with customers on two ends. It's rather amazing sometimes that it all seems to work. Costs are going up, prices are going up, but margins keep getting thinner. Blood centers are investing more in soft disciplines like never before. Blood centers didn't need marketing, communications and donor recruitment personnel in the past. Donor recruitment consisted of scheduling donors and blood drives. Blood centers now need to adopt increasingly sophisticated marketing and donor recruitment regimes just to stay even. Blood center executives are paying for things that they never had to pay for before, and, heck, blood center executives are being hired for their expertise in these areas, rather than their technical knowledge.

The days of just parking the bus down the street and gladly taking whoever happens by have long passed. Blood centers cannot afford to hold costly, inefficient blood drives regardless of the need. Blood centers carefully and methodically

allocate the resources in ways the U.S. military's materials assistance command would be proud. The flip side is that donors and sponsoring organizations do not always understand this. After all, the folks who work for the Blood Center are all volunteers and all the materials are donated.

The typical donor or potential donor has no idea what it takes to recruit, collect, test, process, store, and distribute a unit of blood. The popular refrain is, "Well, I guess you just don't need it bad enough." In planning a blood drive, a blood center will typically recruit one-third more donors than units it needs because it knows that 20 percent of the donors are going to turn over every year. That means 20 our of every 100 donors are going to be new, people you never saw before. Add to that the no-shows, the deferrals, the outdates, and instead of 20 donors, you're recruiting 33.

Blood centers are struggling to control cost through the appropriate mix of fixed sites and mobile sites, but fixed sites, while less costly to

operate, tend to make blood donation less convenient. So what to do?

The days of scheduling staff whenever and wherever are gone for good. Staff wants and expect to have a balanced life. Fixed sites tend to support stable and consistent scheduling, and this is an issue that will cost the blood center employees. Staff turnover is costly and will result in poor customer service, which of course, costs donors. Blood centers are very much in a Catch-22 situation. Again, down in Richmond on Monday, they told us that last year they turned over 35 percent of their collection staff. That's a significant number of people. Think about that at your company or my company. It's unbelievable.

Donor needs. We know more about our donors than we ever have before, but we have much more to do, particularly with new potential donors. What we are learning is that donors want the relationship between them and the patients they serve to be more real. Blood donation is too abstract. The donor today is giving to help

someone they know, not to an institution, or not just to give. We know that donors will respond to the right message given at the right time, and provided that the whole process is convenient for them. Timing is everything. Donors expect a good experience, and are much less likely to return after a poor experience. Customer service professionals tell us that a consumer who has a bad experience will pass their tale on to 10 people. We have no reason to think that that logic does not apply to what we do as well.

Donors and potential donors have lots of questions about the donation experience. You know, what is the worst thing that can happen to me? Can I get HIV? Can I get infection? Can I get sick? Will I get a bruise? These are all very real questions that donors ask every day.

Blood centers have and continue to place an emphasis on corporate and community blood drives. Corporations are beginning to push back and cut back. Blood drives are not without a cost to the company. Blood drives are not free. We

know that most of the new jobs created today are by small businesses that can no longer host blood drives on their own. How do we get those people in the door? Blood drives we know are sometimes an issue that creeps into labor/management negotiations. Note, just a few weeks ago Verizon Wireless in New York. They were willing to hold blood drives at their facility, but they weren't willing to give people time off to donate.

Experience again in Minnesota. We worked with Northwest Airlines, who was and is Memorial Blood Center's best corporate sponsor, but they had classes of employees that could donate blood. Machinists and maintenance workers, reservationists could not. We would get calls from dozens of reservationists during the blood drives, who were mad at management, but who were also mad at the blood center, and they weren't willing to donate off the clock. So we know for a fact that it was an issue that came up when they were negotiating contracts. So it's an issue that all blood centers have to deal with. Certainly, schools, community

organizations, places of worship, all present the blood center with challenges that are unique to them.

Now, this is the good part. The major blood organizations are cooperating like never before to bring in donors. In a sense we are working together nationally to make the pie bigger, while the American Red Cross and the ABC Blood Centers compete vigorously to divide the pie into pieces. But I think most of us would agree that competition is healthy.

Corporate America Partners for Life: Baxter, Chiron, Haemonetics, Johnson & Johnson and Ortho Diagnostics are working together to build senior management support for blood donation by leveraging their contacts. Right now we have a pilot project going on in Boston, and I believe projects are scheduled for San Francisco and Chicago in the very near future. I know the goal of this group of five is to involve other pharmaceutical companies and then to roll this program out to blood centers nationally. Blood

drives are more effective when a grass roots employee effort is supported clearly and forcefully by senior management. This program is based on a program that was launched in 1998 called Rx Partners for Life. It was a Johnson & Johnson program with the Health Institute of New Jersey and America's Blood Centers.

The Secretary's Challenge. Secretary Thompson is committed to blood donation along with organ and tissue donation. This is a national effort to involve the entire Executive Branch and all Cabinet officers have signed on to the program. Right now the program exists mostly inside the Beltway, but soon it will make its way out into the field.

We had that planned, didn't we?

Workplace Partners for Life. This is another initiative by the secretary, managed through HRSA. The organizations that commit to this initiative make a commitment to support organ tissue, marrow, as well as blood drives. While many of the several hundred organizations are

already committed to these causes, they have publicly said that they will do more.

National Awareness Campaign with the Ad Council. This is an effort that I think all of us would agree will get us excited. I know it really gets me excited. We've been working for, working together on this project for a long time, and it's finally, it's finally going to happen.

This is a collaboration between the American Association of Blood Banks, the American Red Cross, America's Blood Centers, and the Ad Council to raise awareness of the importance of blood donation with young people between the ages of 17 and 24. It's a 3-year commitment. We know that the average Ad Council campaign will return to us $33 million in media, and that's the average campaign.

And our vision is that blood donation will be a part of pop culture, think in terms of "Only You Can Prevent Forest Fires," you know, "Friends Don't Let Friends Drive Drunk" and "This is Your Brain on Drugs."

We will utilize both traditional and nontraditional media. Obviously, we're playing to a younger crowd, and there will be a grassroots component to the campaign that will allow all of our blood centers across the country to be involved.

My Blood-Your Blood is an education program on the biology of blood and the circulatory system, targeting elementary and middle school students. A high school version is in development and a Spanish-speaking version will follow soon after. The program not only educates young people about blood, but also encourages them to become blood donors, and then of course to encourage their parents and siblings to become involved as well. And this is a program that can be integrated very nicely into the science curriculum.

ABC is also involved with a number of national organizations to hold blood drives and build awareness for the need to donate blood.

It's a great commercial.

[Laughter.]

DR. BRECHER: You should have made it closed captioned.

[Laughter.]

[Commercial played.]

MR. CASWELL: Shucks. Sorry about that.

The Member Donor Initiative is an integrated marketing communications campaign developed nationally, but implemented locally. Key elements include research, targeting data, mass media, direct mail, public relations, and currently we are working with our member centers to build an MDI-like campaign targeting people of color.

I'm going to skip around a little bit here and come back to the stoplight feature, I think. Right now, we're involved in a partnership with Microsoft that involves the on-line scheduling of donors, both at mobile and fixed sites, and the donors not only have the ability to schedule on-line, but will also receive communications from the blood center by e-mail as well.

You've probably heard about the stoplight feature before. This is a snapshot of the blood

supply on any given day. We have the ability to track inventory, but whether or not we want to add that element is under some discussion. This is a little bit about how stoplight works. But you can go to our website any day and pick up this information.

The green is inventory three or more days, the red is one day or less, the yellow is somewhere in between, and there are a small number of centers, not the same centers, but a small number of centers who do not always report their results. But I guess I assume, and maybe incorrectly, that these folks must be doing okay if they don't, if they don't need to report out, I guess.

This is our website. It's very user friendly. It's very much oriented towards the public. You can see, you can check on the, check the blood supply, if that's what you want to do. You can also click on the United States map to find your blood center.

You also have the ability to go into the website and put in your Zip Code and find out the

nearest donor location to you, regardless if it's an ABC or an ARC center--clearly, ABC first, but if there's not an ABC center, then you get an ARC center. But you can do that through your Zip Code.

I talked a little bit earlier about our 1-800 number--1-880-USBLOOD. Blood donors can locate their nearest blood center, either with Area Code or Zip Code. Spanish- and French-speaking versions are nearly completed and about ready to be rolled out.

I also want to mention automated blood collections and donor management becoming much more sophisticated, as you know. This allows for the most efficient recruitment of donors and the best utilization of components. You know, if you're like my wife, you're an AB-positive, they don't want her red cells any more. They want her plasma, and the blood center will do a good job of recruiting her. If they haven't done it in advance, they'll make sure that they do a good job when she's at the donor site.

Interactive technology. You see, and I

know this committee has considered that in the past, it's more efficient. It helps to eliminate errors, which may result in the wrong donor getting through. It demonstrates sophistication to the donor, and it's a lot of fun.

I also want to mention a contingency agreement with the military. I know in the last presentations we talked about inventory movement in a disaster scenario. The agreement that we had with the military we believe is a model for future scenarios. We set up a hub-and-spoke system, which allowed for the quick and efficient movement of blood between community blood centers and the military, and this is our model to move 50 percent of the blood supply from community blood centers around the nation, as needed.

But the short-term outlook, our expectation is that the current state of affairs will continue in the short term, maybe three to five years. Prior to 9/11, we had a supply of three to five days. Now, we are routinely at two to three days.

In the long term, as blood centers work their plans, as we get better and more sophisticated in what we're supposed to be doing, we're confident that we will continue to meet our nation's blood supply needs, routine and/or emergency.

I guess the parting question I have, in thinking about this presentation, and clearly don't have the answer to, but what is an adequate blood supply. And when we're talking about emergency preparedness, what does that mean, and who's going to bear the cost of that preparedness, and how are we going to manage the communications, and the public relations that go along with that.

So, with that, thank you very much. It was an honor and pleasure to be here, and I appreciate the opportunity.

DR. BRECHER: Thank you.

We have time for one or two questions.

Lola?

DR. LOPES: I'm in the business, in part, of recruiting new college students to a major

university, and that is also a very expensive business, and we're dealing with an important generation for you.

I'm glad to see that you're moving into Internet scheduling, but I'd like to suggest that you seriously consider doing more of the communication that would be done once the person shows up at a site, the secured sites on the web. For example, you want to avoid wasting your time and also the time of the donor for something like a person who's been in Great Britain during the critical period or for too long a time.

At the beginning of an interaction, you can basically discover, and without hurting anyone's feelings, explain and turn away people that you can't use right now. But also you can, we routinely now collect all of the basic information about people on-line, and they can start today to fill out an information form--if they're called away, they can come back to it later. This is all password protected--for things that you don't have to have a medical person actually collecting the

information.

Kids love it. The self-service aspect of the Internet any time, anywhere is great. And because you deal with sensitive questions, it's also of interest that we've known for many, many years that most people feel more comfortable telling a computer about personal things than they do telling another human being.

I really think that, although computers seem to be impersonal, and perhaps for your older donor base, they wouldn't enjoy this, I think the younger generation likes this kind of interaction, and you've basically been in a world where you don't have to keep asking them what their date of birth is; that you have a record on them and all they have to do is update what's recent. I think, for your younger generation, that that really is the way to go.

MR. CASWELL: Thank you.

DR. BRECHER: Jay?

DR. EPSTEIN: I guess it's as much a comment as a question.

One thing that struck me over the years is that we don't have donor organizations in the United States, some of which exist in other countries, and other countries have found that peer pressure among donors is a good way, both to recruit donors and also to maintain lifestyles that are conducive to being suitable donors.

And I just would wonder if you have any comments about why we don't have sort of a bottom-up system, a grassroots system, where, instead of trying to recruit the donor, you know, the donors are coming to you, and what it would take to stimulate that environment here.

MR. CASWELL: That's an interesting and a great question, and I don't have the answer to that. I will answer the question, though, that blood centers are, the tension at a blood center, as you know, is between balancing the needs of the patient and the donor. And I think blood centers are now beginning to recognize that they need to have donor advocates, people who actually do talk to donors.

If you change the hours at a blood site, they've got somebody that they can go to. If you changed a question on the questionnaire, they have somebody that they can go to, and talk to and complain. If you change the cookies in the cafeteria they can go to, and they have somebody to talk to.

I suspect part of the answer, though, to your question is I think it's probably more generational how people respond, and I think we have identified in our focus groups for the Ad Council campaign that peer-to-peer contact will be more, will be more relevant than maybe it is to someone my age or your age or someone else. So I think it's a wonderful comment.

Thanks.

DR. BRECHER: Larry Allen?

MR. ALLEN: I appreciate your comments, especially the issues about diversity. Just one of the things that I know I would like to comment on, if we could, for a minute, just forget about the issue of trust in some minority communities and

just talk about getting people to donate blood today.

I'll give an example of some people that we met once that worked in a factory. They gave an example of walking down the hall and seeing someone a little further down the hall that was white, and there was someone in a doorway asking for donors; you know, do you have time to donate? And they asked this person, they went in to donate or at least they talked about it.

When the minority people came down the hall a few seconds later, the person asking for donors didn't even look at them, let alone ask them if they wanted to be donors. So, of course, this caused some problems. They weren't necessarily sure if they wanted to donate, but they certainly felt that they should have been asked.

So I think it's just a lot of issues. It's not just on trying to get the people within that community to know that there is a need, a definite need for their blood, but it's also the people that are looking for those donations to

maybe look at things a little differently in how they approach people because that has a lot to do with it.

And I know I heard you talking about looking at ways to increase donorship in minority communities, and I would love to hear more about that because we try to talk to people about donating, especially issues of sickle cell. I've been working with Dr. Sandler on some things over the years just trying to update families and parents on the need for these things.

But there really is this issue of trust that just has not been overcome. And I know one of the ways of trying to overcome it is to be consistent and to be there when these people are trying to do, you know, church functions, things of that nature.

I don't know what your plans are, but there's got to be some different approaches to these communities because there's a real issue of trust that I'm surprised it's still as strong as it is today versus 20/30 years ago, but I guess you

guys realize it is just as bad today as it was 30 years ago, and it's something that we have to overcome.

MR. CASWELL: Well, we'll certainly get you involved in our effort. So I've got your name, and I've got your address. So we'll keep you involved.

And I think some blood centers are out there right now doing a pretty good job at reaching out to people of color. But as you pointed out, it's not easy. We're talking about trust issues that go back.

Many blood centers work with the National Marrow Donor Program, and I think that the Marrow Program, I know the Marrow Program realizes that it needs to have more people of color in its registry, and they partner very close with blood centers. And it's a good, strong partnership. So that's one way of attacking the problem--approaching the problem in the short term.

Another way is I think blood centers are recognizing that if you're going to have someone go

out and talk to African Americans, it's probably more effective that the person be African American or be, you know, Mung or Laotian or American Indian or whatever, that that's more effective recruitment.

The blood center makes a commitment to employing people of all colors. I think that goes a long way towards building that trust, too, but it's not an easy problem, but it's one that obviously we need to figure out if we're going to, if we're going to build any kind of reserve in the future.

Thanks.

DR. BRECHER: We're going to move on. We lost some time, for technical reasons, earlier. So we'll see if we can catch up.

We're now going to hear from Alan Ross from the American Red Cross.

MR. ROSS: Well, thank you. Good afternoon, Mr. Chairman. I'm Alan Ross of the American Red Cross.

One of the disadvantages of presenting

this late in the program is what I'm going to say has probably already been said today. I guess one of the advantages, it might help shorten the program so you can get out earlier, but hopefully I'll have something to say that will be a little bit different than what's been said earlier today.

One of our premises that we have is that there is a increasing need for more blood donations from more eligible donors of the public and more often. And why do I say that?

If you look at our inventory over the last really a little over a year, every time, the top line here is our collections, the blue is our demand, every time our collections and demand touch, our inventory goes down drastically. In other words, we erode our inventory tremendously every time that occurs, and that's been a problem in our effort to build a strategic blood reserve, either liquid or frozen.

Now, our red cell supply in July of this year is really a little over three-and-a-half days, and that's much lower than it was last year. It's

much lower than it was in 2001.

What's really frightening to me is that we have barely 10,000 units of O-positive on the shelf right now. That's out of an organization that needs 25,000 units a day to meet transfusion needs. Our O-negative inventory right now is just a little over 3,100, nearly 3,200 units of O-negative.

Now, what have we done to deal with this issue? Well, quite a bit, actually. We've been on local appeal and national appeal, but one of the biggest proactive efforts that we've undertaken this year, beginning in May, is the Save of Life Tour Public Awareness Initiative. You may or may not have heard about this. We're investing $13 million in two convoys of four vehicles, visiting 350 cities around the United States that we'll complete here in Washington, D.C., on November 20th of this year.

Now, what's the goal of the Save A Life Tour?

Well, number one, there's teach-ins, and then there is a mobile museum that's a very large

semi that has a history of transfusion medicine and an effort to build public awareness with diverse donor groups and youth. That's really the target audiences.

For many years, we as an industry have not done a good job on building public awareness and education, and this is a major commitment by the Red Cross to try and do that.

In addition, we have undertaken broadcast voice mail campaigns to our existing donors, broadcast e-mail to our existing donors. We have a lapsed donor direct mail and tele-recruitment campaign, both in-house and outsourced. We've developed a Jimmy Carter PSA, a Give Blood Again PSA.

We have web movies, with donor recruitment reminder messages from recipients, that are distributed to regions for use locally; of course, the U.S. Department of Health and Human Services, the Tommy Thompson Give Thanks, Give Life, Give Twice campaign that was kicked off last year; prospective donor cold calling. We're investing in

outside firms to cold call for blood donors; we have urgent donor grams, like a telegram, that is going to existing donors; direct mail postcards for mobile drives; direct mail for fixed sites; blood drive sponsor letters.

And of course we've probably invested another $7 million in paid advertising this year. We have never done this kind of stuff in the past. And in 2002, we invested over $100 million in donor recruitment efforts. Now, that's a significant amount of money, and we're budgeted at about $125 million for FY '04, this coming year.

It's a tremendous investment, but we're still not seeing the returns. And like what Dr. Gilcher has mentioned--the post-Iraq shadow effect, we certainly experienced that. We had plenty of blood in March, and April and in May, but the donations started falling off just after Easter, just after the cessation of the hostilities in Iraq.

And May and June of this year were the lowest levels of donations. We hit about 85

percent of goal. The first time we were that low in about 10 years.

Now, it's bounced back through a lot of efforts. July, we were about 96 percent, and August we were about the same thing. So we are making a difference.

What else can we do to help build a reserve? Well, you know, decreasing the discards, when we discontinued HIV p24 antigen, 6,000 donations now are not being discarded per year because we're doing NAT testing because of the false reactivities with that particular assay. We are no longer discarding the ALT donations because we now have NAT HCV testing.

So 9,000 donations a year are now being recovered, and we have 65,000 donors to go back and re-enter as a result of that.

You know, when we first considered a frozen blood reserve in the fall of 2001, we wanted to know what the public, how they would feel about donating to a frozen reserve. So we commissioned a study by Insight Express, who interviewed over

2,600 individuals.

It was very interesting. Eighty-one percent of the individuals interviewed said they had no interest in donating to a frozen blood reserve--81 percent; 16 percent said they might have an increased interest, and those were mainly women that had that interest; and 3 percent said they probably would have less interest.

But that was kind of a startling statistic for us. So, Dr. Gilcher, I hope you really have, you must have great people in Oklahoma, because if they're interested in donating to a frozen reserve, then that's tremendous.

Pre-9/11, the American Red Cross history in frozen blood reserve was really limited to autologous and rare donors. And I'm not going to go through all of this information, but the limitations of course have been stated earlier: 24-hour post outdates. We really need to get to that 14-day post outdate before it's going to be a functional program.

This is a picture of the ACP 215, which

has been described earlier.

The issue of the open and closed systems have been discussed. Currently, most of the frozen blood in this country has been frozen in an open system with 24-hour post dating.

The relative costs, there's been a lot of talk about that. Red Cross has received millions of dollars in financial donations to support the frozen blood program to develop it. And that's what's keeping us going over the past two years in doing the studies necessary for licensure with the other anticoaganists that have not been licensed to this date.

We hope to have all of the data submitted and hopefully have a program back in place by 2004, but we've essentially put the program on hold until we get this data submitted and approved.

Why is a frozen blood reserve important in our eyes? Well, we have used the 10,000-plus units we froze post-9/11 to supplement our inventory during shortages. And every once in a while, we'll have a demand increase. When we think we have an

adequate inventory, there will be a big demand of O-neg, and this has helped us supplement that O-neg need.

There's also an opportunity to optimize issues of wasted O's, and I'll go through that in a little bit. But the 14-day will allow us to provide a more cost-effective, if you will, frozen blood product.

This is a picture of our current frozen inventory. It's about 10,000 units. The red has been rejuvenated units; the blue were non-rejuvenated units. Our plans were to really rotate through this entire inventory in three years, about 33 percent used every year.

We have this inventory in three primary reserve sites, and our goal is--we usually have about 50,000-plus of liquid. We're down to about 44,000 or 45,000 liquid right now. In April of this year, we had 175,000 units of liquid, which is where we would really like to be.

As I mentioned already, since 9/11 we've used this frozen inventory to augment hospital

inventories and Type O in times of shortages.

In the past, in FY01 we distributed a little less than 9,000 units of frozen blood. This was primarily autologous and rare donors.

Like everybody else, we believe that the reason for a frozen inventory is to augment inadequate liquid reserve because it's not the ready reserve. The liquid reserve is your ready reserve. The frozen is just to backfill.

Our capacity, we can thaw 700 units a day, and with a 20,000-unit inventory, that would give us approximately one month's worth of--we could empty our entire 20,000-unit reserve within one month.

Like everybody else, we have grave concerns about new test requirements, but with retention samples, we can resolve that issue. There is the issue, of course, of adequate specimen, whether you have the right specimen. The biggest question that we face, like everybody else, is the question issue, the donor question issue. I'm not sure how you resolve that because I think

calling donors up and asking them to remember has not been a good experience for us.

So our recommendation, as I said before, we cease freezing red cells in an open system. Once we get approval for 14-day post-thaw dating, we'll re-examine the issue and perhaps go up to 18,000 or 20,000 units.

What we need to go forward is licensure of closed-system freezing and our particular collection set is an anticoagulant. We need more Group Os, obviously, but there could be another source of Group Os.

Here's opportunities for more Group Os. Currently, we discard quite a bit of red cell antibody-positive red cells. The thought is freezing, thawing, and deglycing these units could provide an additional source of Group Os to put in the frozen reserve.

Currently, we have about 9,000 red cell antibody-positive units per year. These may be able to be salvaged and put into the frozen blood program rather than discarded. In addition, we

outdate about 11,000 Group O out of 3 million Os a year. It's a small percentage, but 11,000 plus the 9,000 positive antibody screens could provide the necessary red cells that would give us the 20,000-unit reserve that we're looking for.

Another opportunity is rejuvenation of units. We need to get the studies done, the data submitted and approved, but rejuvenation is another opportunity for us.

Again, the relative cost to freeze and thaw is now less because of the 14-day post-thaw dating. The donations, financial donations that we have received have allowed us to offer these deglyced units to our hospitals at our regular red cell price. And once again, our goal of using a frozen reserve is really as the back-up for our liquid reserve, and it will allow us to minimize wastage of Group O units that are being wasted today.

So, in conclusion, there really continues to be a need for more blood donations, for more eligible members of the American public, and we can

do that through a variety of programs, like I mentioned earlier. I'd also like to thank members of AABB and America'S Blood Centers for our Ad Council campaign that we're moving forward with. It's those kinds of programs and public awareness that are going to help us meet our overall collection goals for the future.

Thank you.

DR. BRECHER: Thank you.

Questions, comments? Jeanne?

DR. LINDEN: In terms of your goal that's still on the screen there, you mentioned the millions of dollars that you've put into reaching out to donors. Could you tell us about the resources that you've put into donors who were inclined to donate to make it easy for them to find a convenient site? The 800 number, my experience with it, since I'm in a Red Cross area and I've called on behalf of my O-negative husband, you get somebody 300 miles away who's geographically challenged, to put it charitably, doesn't appear to own a map, can't find anything close by. I'm

wondering, do you have a website where people can search by zip code and maybe find something themselves that gives the hours and location and so forth that--

MR. ROSS: It is not universally up yet. It is in some regions, but we're planning over the next 12 months to have a universal website that will allow online scheduling of donations, also have the appropriate deferral guidelines so they can know before they even present whether or not they're eligible to donate. But that will take us probably the rest of--another 12 months to complete nationwide. It is in place in some areas.

DR. BRECHER: Jay?

DR. EPSTEIN: Dr. Leparc and others made a very strong case for a better database, knowing where all the blood is. And I just wondered if you could comment at what level the Red Cross system is in terms of knowing the size of the inventory, where it's located, what the hospital need is on a daily basis, and how you use that information.

MR. ROSS: Thanks for the question. We

have 35 discrete databases from our 35 blood regions that are downloaded at midnight every night to a data warehouse that then allows us at 6:00 a.m. the following morning to review inventory by type and by aging in every one of our inventory locations. We don't have a view into the hospital inventory levels at this time, and that's something that I think is sorely needed, because at least half the inventory in this country is in the hospitals, and sometimes more.

But we utilize this system--we have an active inventory management team that then reviews every region that has a particular blood type, and if that blood type is below one day, we will automatically ship from one other region to that region to balance the inventory throughout the system. But it's not an optimal system. Our goal in the new computer system is to have a single discrete database instead of 35, and it has to be realtime, because that snapshot at midnight may be okay.

Now, for instance, every Sunday night we

know that our Monday morning inventory is going to be high, and then the hospitals place their orders on Monday mornings. And we could see a 25- to 30-percent decrease in that inventory by 12:00 noon on Monday. So then it's not really a very accurate picture. So a realtime system is something we really need and are striving for.

DR. BRECHER: Lola?

DR. LOPES: I'd like to harp a bit more on the Internet stuff and encourage you to move just as quickly as you can in this direction. I think of the money that you've put into your more traditional advertising. If you think of receiving a postcard in the mail urging you to do some good thing, I think many of us intend to do it and that we store that postcard over with the coupons from Lenscrafters, all those things that we're going to do later, and find them six months later, or if you hear a public service announcement on television that urges you to go to your local blood center, you think, That sounds like a good idea, I should really do that. But there's no action if it's, you

know, 10 o'clock at night, you're in your pajamas, there's nothing you can do right then.

With a website, basically the announcement says go to www.givebloodnow.org and, boom, you're there, you're already halfway committed to doing this thing, which is a very, very important psychological principle.

Karen leaned over to me after my first mention of the Internet and said that one of the problems here is that the FDA mandates that real live human beings gather the information. I really think this is a place that we should look at the regulations and figure out which of that information needs to be gathered on the spot by a real live human being and which of it really can be gathered without that, safely. Obviously, safety is our first charge here. But to move quickly to get a website that could answer the question where in my area is there a donor center, all you need is something just like the weather sites on the Web where you type in your zip code and, boom, an address comes up. That's not a 12-month project.

I think some of these things really should be rolled out on a quick schedule, even though the rest of the database obviously will take a long time to come up. This is something where the Internet forces you to learn to manage rapid change and the rapid requirements of the receivers. We didn't have e-commerce at our university. We outsourced it for a while. But the price went up, and within three months we had to develop our own system for handling the Visa charges. And if we hadn't done it, we would have lost customers because the kids now and their parents are expecting this kind of thing.

DR. BRECHER: Celso?

DR. BIANCO: Just an addition to Lola. The solution, Lola, is to have the manufacturers of computers to incorporate the blood bank into the computer.

[Laughter.]

DR. KLEIN: I have two questions for you, Alan. The first is: How centralized or decentralized is your frozen inventory at this

point?

MR. ROSS: Our frozen inventory is isolated to three locations, at least for the strategic frozen reserve. Of course, we've got frozen products in probably 30 of our 35 blood regions that are rare-donor frozen units.

DR. KLEIN: And the second question: I really want to commend you on the $125 million for public awareness. I think that's a real paradigm change for all of us and an important one. What percentage of your blood budget is that?

MR. ROSS: It's not enough. It's about 6 to 7 percent. We're about $1.7 billion right now.

I want to touch back on how we're spending that money. We're trying to get smarter in how we spend that money and have retained an organization called Veritas. Some of you may know of Veritas. Veritas will tell you by zip code the psychographics of the population by zip code, will allow you then to market to that particular demographic group with targeted channels that may reach them more effectively than we are now. For a

high-tech person, for us to send them a postcard is not very smart. And for a low-tech person, to send them an e-mail when they don't even have a computer is not smart. So we've got to balance that out.

DR. BRECHER: Karen?

MS. LIPTON: One other thing. I wanted to return to what Jeanne said. The National Blood Foundation actually had a significant amount of money put into a study of blood donor motivation, and actually two of the things--and it's not quite finished and published yet. But two of the things that are popping up as the greatest deterrent: number one is a bad experience at a center. So putting money into that whole thing that Scott was talking about, about customer orientation is critically important. The second thing was the questions and that there are just too many. That was really operating as a deterrent for people, and so I really think it's a message to us to simplify, simplify, simplify the donor process, including what we ask them when they come in the door.

DR. BRECHER: Jerry?

DR. SANDLER: I'm in a hospital that's supplied 100 percent by Red Cross, and I was in the room when the Red Cross representative not too long ago said, "We'll put in leukoreduction; it's only going to cost you about $6 a unit." And it was very slick. And then, of course, we got a double-digit increase in our price. And today you come and say, "I'm going to solve all your problems, and it's not going to cost you anything."

How are you going to put in all of these washers and all of this stuff and it's not going to cost any money?

MR. ROSS: We have already--the washers, freezers, have all been purchased, much of it with donated funds from individuals and from foundations. So that money is spent. And it's not--you know, we're not talking about a huge program in the scheme of things. We're talking about an 18,000-unit reserve with a rotation of 6,000 units a year out of over six million.

DR. BRECHER: Okay. If there are no more questions or comments, thank you.

We're going to take a 30-minute break. We'll be back at quarter of 4:00.

[Recess.]

DR. BRECHER: The next thing we're going to discuss are FDA regulatory concerns, and Betty Poindexter is going to talk about product storage.

MS. POINDEXTER: I changed it slightly to have it address both the scientific and regulatory concerns. Some of these issues were alluded to earlier by both Commander Bartley and others.

This is a quick overview. We're going to look at licensable liquid stored products, licensable frozen stored products, what I have called investigational. It does not mean that they're under IND. It just means that they are out there probably used by medical practice, but not necessarily something that is under IND at the FDA. The starting material of both the red blood cell product and the platelet product, some of the processing issues, storage, transfusion doses, product safety, and some conclusions.

Currently, we have licensed liquid stored

products that include an array of whole blood, red blood cell products, apheresis platelets, as well as random donor platelets, and an array of plasma products. Investigational products include apheresis granulocytes and pooled platelets that are liquid stored and frozen stored products in the future perhaps of random donor platelets, apheresis platelets, and pooled random donor platelets.

The starting material for red blood cells is very dependent on the anticoagulant selection, the whole blood volumes that are collected, and what I've put in parentheses is the current acceptable range for the two different blood collection volumes that are out there, the 450- and the 500-ml volumes that are plus or minus 10 percent, the 405 representing the absolute worst case.

The red cell mass issues, total hemoglobin, we as a blood organization and the FDA have not come down on whether we want to define a particular total hemoglobin per unit at this time. We have leukocyte reduction and the timing of that

leukocyte reduction, whether it's done rather immediately after collection at room temperature or whether it's performed later, perhaps 24 hours to three to five days after collection after being stored at 1 to 6 degrees Centigrade.

These are some questions that we have. What effect does the product age at the time of further processing have on the final RBC product? Does it matter whether it's three or four days old or 25 or 30 or 42 days old? Are there data to support that? What effect, if any, does gamma-irradiation have on those red cells prior to further processing? Does the base anticoagulant, again, have any effect on the future processing? Currently, as was alluded to earlier, CPDA-1 is the anticoagulant that many centers use, although in the AABB tech manual they do list CPD as an acceptable base anticoagulant. So we've already gone there.

Can RBCs be stored longer than six days prior to glycerolization? Does the timing of the leukocyte reduction play a role in this? Will it

make it a happier product at the end of the processing? What role do the novel anticoagulants and anticoagulant combinations play? We now have red cells that are collected both in--automated red cells that are collected in CPD, CP2D plus AS-3, and now we have two devices--three devices, actually, that are collected with ACD as the base anticoagulant with various additive solutions, currently both AS-1 and AS-3. Do those play a role in how those red cells will store prior to further processing into a glycerolized product, or do they have no effect whatsoever?

People have talked about the rejuvenation process. Does RBC rejuvenation have a role to play? Can we take those units, irrespective of their base anticoagulant, and put rejuvelsol or another sort of rejuvenation solution in and have those products function properly after being stored in a frozen situation?

One caveat with the rejuvesol solution is that it was meant for a 450 ml collection, and there was debate earlier on, particularly during

9/11, as to whether there was adequate rejuvelsol in the bottle to be able to adequately rejuvenate 500 or 550 ml units, and we have no data to support that at this time. Those studies may be ongoing.

Do the red blood cell additive solutions have a role in the pre-glycerolization process? Currently, the additive solutions have to be added within 72 hours of collection. If you then go on to process that unit at day five or day six for glycerolization, did that have a beneficial effect or a deleterious effect on those red cells? Does the red cell mass influence the process? Are there adequate processing solutions for the wide range of red cell mass encountered during whole blood collection and processing?

These have been also alluded to today. We have this divergence of freezing temperatures, the effects of minus 65 and minus 80 C on the final red blood cell products. Is there a difference? Is there published scientific evidence to demonstrate similarities or differences in these two different temperatures? The frozen shelf life, the shelf

life varies from three years to ten years depending on the glycerolization method, the anticoagulant, and my understanding is whether it's been rejuvenated or not. Many people have addressed the frozen serum plasma repository for future testing of those products once they've been frozen.

Container integrity. Is the container--the final container, the storage container for freezing--how has it been selected? What is the fill volume that will allow proper handling and processing and as little breakage as possible? Today was the first time I had heard a number of 15 percent fracture rate in those bags. That's astounding to me. That says that there's either weaknesses in the bag, or there are strong weaknesses in the handling of those products for further processing.

We've talked about after deglycerolization the storage time at 1 to 6 C, the 24 hours versus up to 14 days. People were talking about closed-system processing. It is not a closed system. It is what we've termed a functionally closed system

because you're using a sterile connecting device to attach fluids in final storage bags, and it's also using 0.2 sterile barrier filters. But it is not an integrally attached set with absolutely no openings during the processing. So it's truly a functionally closed system, rather than closed.

Again, what are the final storage containers, the final storage and resuspension solutions? Someone earlier had addressed the 0.9 percent saline and the 0.2 percent dextrose. That's different than the AS-3 solution that's currently with the Model 215 from Haemonetics. Are there differences? Could the storage solution, could the saline-dextrose solution give you similar dating? We have no data to support those conclusions, so those studies would be welcomed.

This is a slide on diminishing returns. This is taking the worst-case red cell unit and processing it through to a deglyced resuspended product and accounting for a low-volume collection. And if you leukocyte-reduce the product and lose 15 percent, which is what we've allowed through our

guidance, maximum of 15 percent, and you go on to glycerolize and deglycerolize that unit, and you may lose anywhere between 1 and 20 percent of those red cells through this process, then you have additional hemolysis during your 1 to 6 degree storage, whether it's 24 hours or 14 days. And citing a worst-case example with a 450-ml draw from a donor with a 38 hematocrit, you have approximately 154 mls of red cell mass, or 51 grams of hemoglobin. If you subtract from that the 15 percent maximum loss through leukocyte reduction and then the deglycerolization loss, you end up with 104 mls of red cells or 34.6 grams of hemoglobin.

So rather than perhaps a patient receiving three or four units on their monthly transfusions, assuming perhaps a sickle cell recipient, they may now need to receive six or perhaps seven units to get the red cell mass equivalent of products that might not have been frozen deglyced and may not have been leukocyte-reduced, depending on the procedures in place.

We have product safety concerns, one of them being red blood cells and bacterial detection. Do the current test methods allow for the detection of microorganisms in frozen red blood cell products? Have those methods been tested?

We now know that there's a lot of experience with using various automated technology, automated bacterial detection technologies, for discovering bacteria in platelet and platelet pheresis products for QC testing. The instrumentation that is out there now has never actually been validated on frozen red blood cell products, and that's just food for thought.

Are there adverse effects of the circulating red blood cells and red blood cell membranes after freezing and deglycerolization and storage for 24 hours to 14 days?

My understanding is that the processes will alter the membrane of the red blood cells and may cause deformability problems. They may not be able to deform as easily as what a native red cell might be, and that's just a question. We don't

have the data to support that. The studies have not been done. And are there thrombogenic potential for these circulating red blood cells and red cell membranes? Receiving two or three autologous units for hip joint replacement is not the same, perhaps, as receiving four to six units a month if you're being constantly transfused for the rest of your life.

We're lacking in vitro data, comparing frozen red blood cells stored for one day versus red cells stored for 35 to 42 days with some of the various anticoagulant solutions that have not been studied to the fullest extent.

We would like to receive in vivo autologous radiolabeling studies to demonstrate normal donor satisfactory survival and recovery. And of course, as always, in those final products, a hemolysis of less than 1 percent at tend of the storage period.

The starting materials for random donor platelets, again, may be anticoagulant dependent. We've seen studies on platelets, but they've

usually been in vitro studies and radiolabel recovery and survival, but are there differences in those anticoagulants? Will they make a difference in how those platelets store for periods of time and will they make a difference if those platelets go on to be frozen?

The whole blood collection volumes for random donor platelets, again, vary considerably. The platelet mass recognized in the regulations all units should be greater than 5.5 times 10 to the 10th, but with the 500/550 mil collection volumes, we are being told that levels can be up to 1.3/1.5 times 10 to the 11th platelets, which is a sizable difference and stored in 45 to 65 mils of autologous plasma from that particular donor.

Again, we have the time of leukocyte reduction. Can it be as soon as two to eight hours after collection at room temperature? Could it be within 24 hours after collection, when the platelets, whether they be random donor platelets or apheresis platelets that go on to filtration, can they be filtered at 24 hours, and are they

happier then than they might be at two to eight hours after a vigorous resuspension?

There are filters that have been cleared for filtration within 3 days of collection. There's also the issue of do you leukocyte reduce after pooling. There are filters that are there that allow one to pool up to five or perhaps up to ten random donor platelets.

Does the platelet age make a difference at the time of further processing? When you have a random donor pool, do you pool four to six or eight different units of platelets and their native plasma or do you select, as in Europe, just one particular plasma to resuspend those four to eight units in? These are questions that we don't have answers for yet.

How soon after resuspension and collection should platelets be frozen, whether they be random donor platelets or apheresis? We have no clue. The platelet data that I'm aware of is so old that we're just not there.

Are there effects of gamma irradiation on

the previously frozen platelets? If you don't irradiate the platelets up front and the freezing creates some sort of injury to the platelets, will the gamma further damage the platelets? Again, we don't know those answers; the effects of freezing on previously frozen, previously gamma-irradiated platelets.

What is the total percentage of platelets lost during the processing? I've not seen those numbers.

Does platelet mass influence the processing? Again, is there adequate processing solution for the wide ranges of platelet mass that might be encountered during whole blood, random donor platelet processing or apheresis collection and processing?

Does the cryo preservative solution have to be removed prior to transfusion? In the olden days, 25/30/35 years go, with DSMO, there were some people who washed out the DSMO, and there were others who swore that you didn't need to remove the DSMO, although the room and the patient, you could

identify the patient very easily by walking onto the nursing station.

If the processing solution has to be removed, what percentage of the platelets are lost through this processing?

What's the final resuspension solution for the platelets? Is the volume sufficient again for the wide range of platelet mass encountered during the various processes? What is the final storage container for random donor or frozen platelets? What's the platelet capacity of that bag? If it's a 300-mil bag, it has a limited capacity, a 600-mil will have a limited capacity, a liter or 2-liter actual platelet storage bag may have a different capacity than a standard PVC bag.

Are the container integrity issues the same issues that are there with the red blood cell and with other products that are frozen? Do they break? How often do they break? If we're counting on any sort of frozen back-up system, we need to have these addressed. Again, the final storage container, the size and the materials, whether it's

an actual platelet bag or whether it's just a large PVC bag, the integrity and the storage capacity of those bags will have to be tested.

Open system versus functionally closed system processing. Currently, my understanding is that when you add the DSMO, you're adding it as an open-system process. But if it were a functionally closed system, might we be able to get a longer shelf life off such products?

Currently, my understanding is, once the units are processed, and I realize these are rare events, they're transfused immediately after processing, but could a functionally closed system give you four hours or perhaps even 24 or greater hours of storage? Again, we would need to update it to support these types of conclusions.

Platelets and bacterial detection. Will the current test methods allow for detection of microorganisms in frozen platelet products? Fully understanding that bacteria freeze as well as platelets do, perhaps better, and they might proceed to grow after they're thawed and

resuspended in whatever the suspension media of choice is. That's data that we're lacking.

Are there adverse effects of circulating platelets and platelet membranes? Are there thrombogenic potential?

Platelet data that we would be interested in seeing would be in vitro platelet function studies comparing frozen stored products to fresh day one platelets and comparable comparability to liquid-stored platelets. We would be interested in in vivo autologous radiolabeled studies in normal donors, demonstrating satisfactory recovery and survival.

And, currently, what we've been seeing are liquid-stored platelets compared directly with two different labels to whatever the test is to a control product. And what we're discussing currently is taking the test product and a fresh sample from the donor and radiolabeling those platelets and following their survival and recovery and having a more direct comparison. This is using a model that Dr. Murphy presented to us last summer

at the Bacterial Inactivation Workshop.

The routine use of frozen platelets may require a controlled clinical trial demonstrating safety; primarily, the absence of prothrombolytic adverse effects. We would also be looking for hemostatic effectiveness, hemostatic function, and hemostatic function in thrombocytopenic patients. And also there may be special uses for these products, maybe not day-to-day transfusion in thrombocytopenic patients, but perhaps specific trauma or surgical situations.

Platelets and bacterial detection pooling. We know now that we have bacterial testing methods that will monitor bacterial growth in platelet products. We currently use that testing for quality control, but there has been discussion at numerous meetings now about perhaps using that similar testing for release of products, but we would be looking for additional data.

Using those methods, then one has to consider whether you're testing individual units or whether you're testing pools, when you actually put

those products on test, whether it's day one or day three or sometime later, and whether or if you have to retest those products at some time point in that storage.

Bacterial testing may allow us to extend the shelf life of platelet products, whether they be random donor products or apheresis, to seven days.

Again, with the random donor platelets, we have that final storage container issue and what the pool size is. And those containers would have to demonstrate satisfactory maintenance of pH throughout the storage period, irrespective of whether it was five or seven days, and satisfactory maintenance of cell function. These would be in vitro studies.

The timing of the pooling. Should it occur immediately after processing, within 24 hours of collection or, as it is now, just prior to administration?

The conclusions. Frozen red blood cell and platelet products should have safety

demonstrated prior to their routine use. There are many basic questions that still need to be addressed, but we do have the tools to answer those questions. Bacterial testing of platelet products, and these are room-temperature, liquid-stored products may lead to the extension of the current five-day dating period.

A question to everyone is, is it time to perhaps set a minimum product recommendation so that we know what our starting material is, so that we can anticipate perhaps what our final product to the patient might be?

A lot was said about the Model 215, and its advantages over the old Model 115 device, but we need to have these processes validated prior to putting them into routine use because we found, during 9/11, as a lot of people mentioned, that they were problems with availability, both with the devices, with the kits, with the solutions, with the freezers. We don't want to go into this blindly.

And what happens if the lights go off?

This is relating to New York? I mean, if you don't have electricity, if you aren't on an alternative power supply, you can always have liquid-stored blood in freezer chests with ice on them. But if you're depending on huge freezers, and you're cranking your power for some extended period of time, if there are traffic situations where your truck can't get there with the fuel, you're going to lose your products, again.

And I would like to thank you.

DR. BRECHER: Thank you, Betty. We have time for one or two questions or comments.

Keith?

DR. HAAS: Yes, I just wanted to emphasize, at least from my own experience, that the platelet function aspect of it is just an incredible hurdle compared to function of red cells, at least we were involved in an autologous trial from FDA-approved thrombopoietin stimulus, with very, very high pressure and very, very minus 180-degree Centigrade.

And the receptors were preserved on the

platelets. We could cross-link them really well, but I tell you, getting endogenous platelet release, it was not zero, but it was like 20 percent of what it was in those same samples pre-storage.

And I think we've got the technology, and you alluded to this, we have the technology, even before we do in vivo studies, I think, to assess, and I think that should be, you were asking for suggestions about what sort of standards, I think that, including platelet spreading on EM, and things like that, that really indicate, before we go too far down with a particular technology, that the in vivo function is at least there, probably because you don't--the worst-case scenario is to store platelets and have somebody who's bleeding from thrombocytopenia, obviously, and then just get a fraction of the expected response, even though you get the incremental response you expected.

DR. BRECHER: Celso?

DR. BIANCO: Yes. First, I want to thank you, Betty, because I think it's the first time

that I see the whole picture from your side--very comprehensive. I think that this should be published in some format because that's almost a guide on the questions that you are going to ask.

MS. POINDEXTER: Thank you.

DR. BIANCO: And so I thank you for that.

The point that I would like to raise is that when we look at this incredible amount of information, and I'm not going to talk about frozen platelets. I leave this to Keith. It is scary for a manufacturer of a product or for a center that wants to create some small change in a product to look at this without having attached to it a kind of a set of priorities.

For instance, there are things that we have from experience; that is, the changes between 450 and 500 or the calculations on how many platelets are going to be there, I think everybody has a lot of data. And upon request, I'm sure that most of the centers will be glad to provide it to you, digest and analyze or raw data that could give you that without having to be the burden of a

manufacturer to try to do it.

The other type of thing is I wonder if, as the FDA tries to prioritize those things, is to look at all of these requirements and see which ones are essential; that is, which ones could create life-threatening situations. And, obviously, the questions that you raised about bacterial contamination, I would put in this category versus others that are more a question of dosage; that, by experience, we've lived with for--I never knew how much I'm giving a patient, in terms of red cells or platelets, and essentially what we all learned to do was to measure it after the effect and see how the patient responded and go.

There could be, if we want to harmonize and all of that, that addressed in Phase 4, post-licensure-type studies and things so that we would facilitate the introduction of new anticoagulants, new materials or new things.

And I really commend you, but I also would like to emphasize that, with prioritization, this

would not be scary, and this could encourage people to do the right thing in order to get new products up.

DR. BRECHER: Andy?

DR. HEATON: Andrew Heaton.

In terms of the standards that you just listed, I think it's helpful to review the chronology here. The issue we're discussing today, which is emergency preparedness, raises the need for frozen product if you want to have an inventory available for a long period of time.

And what you've just raised, Betty, is the fact that the original frozen product data was generated long before a series of other changes occurred. So red cells and DSMO platelets are 20- or 30-year-old products, and then in the last decade, we've added AS-1, AS-3, AS-5 different plastics, about three different plastics, leuko filtration and irradiated red cells.

So we've never, in fact, gone back and linked the more recent developments in cell processing with the older developments of frozen

storage. So one recommendation I would make is that the FDA do publish guidelines, where it would like to apply the standards, developed as a result of the more recent solutions, to the criteria that you expect to see of the frozen products. So that would be my first recommendation.

Secondly, it's very unusual in that for red-cell products, especially, the FDA has no product specification. You don't specify what has to be in the red cell unit. The only specification is the hematocrit of the donor and the weight of the unit. But the reality is that there is no final product specifications. Many European countries do have such specifications, and I think that you would do the manufacturers a great benefit if you published a content specification, which will be very useful.

And then, lastly, a third observation I'd make is that, although for red cells, there's a 75-percent post-transfusion recovery standard. There is no such standard for platelets. And so I would very much support Dr. Murphy's suggestion that the

two-thirds standard, relative to a contemporaneous control fresh platelet would be very, very useful and would allow the manufacturers to set the specifications to make products that would allow the blood community to meet the needs of an emergent requirement.

MS. POINDEXTER: Right. And that's one reason that I brought this up. Dr. Murphy did present it last year, and my understanding is that something to that effect will be published soon. And we would like to discuss that with the manufacturers to get buy-in.

And another point, you said that a lot of our data is old, and that's one of the other problems that we have is frequently people are comparing today's product, with all of its bells and whistles, to something from 1980 or 1985, and that's a major problem because products have changed so much, including the leukocyte reduction, but just the product volume collection and everything else, and it's difficult.

DR. HEATON: And it will be helpful if you

could simplify those.

MS. POINDEXTER: Right.

DR. HEATON: Because that list you gave is a huge, long list, quite daunting to a manufacturer contemplating meeting those specifications. So the more you simplify it, it will be very helpful.

MS. POINDEXTER: Right. If I could go back to something that Dr. Bianco said about, let's see, it was about the blood centers providing us with data, rather than putting this burden back on the manufacturers.

The advantage, from my perspective, the advantage to having the manufacturers submit that data, whether it's the use of the 215 or whether collections can undergo certain other processes, is that you have one SOP that you're working with or one set of directions.

And when you have numerous blood centers, each thinking that they know best, and they know better, and perhaps never coming to agreement, it's very difficult for us, then, to keep track of 700 variations on a theme. Where, if we can hone in on

Haemonetics or Baxter or Medsep or whomever else, then we have just one set of instructions for use.

DR. BIANCO: You have made a very good point, and I certainly accept it. But if you give us the SOP, we know how to follow SOPs.

And just one comment. There is one more requirement, Andrew, that you did not mention. The red cells have to be red, and the platelets have to be yellow.

[Laughter.]

DR. BRECHER: Thank you, Betty.

Oh, I'm sorry. Harvey, last question.

DR. KLEIN: Before you go, Betty, could I ask you a question or at least comment a little bit? Because we were talking about frozen red cells primarily today, and I'd just like to be sure that we know what we're comparing them against.

There's sort of a difference between safety and efficacy on the one hand and then basic studies that need to be done or that could be done.

I made a quick calculation here, given your example of 51 grams of hemoglobin, and if we

think about 42-day storage in a refrigerated state and lose 10-percent perhaps for filtration, knowing that only 75 percent of those cells need to be viable by chromium labeling, which means that 25 percent are dead on arrival, that comes out to 34.4 grams of viable hemoglobin, and I think you mentioned 34.6 in the frozen.

So, compared to what, is a very important point when we're thinking about those.

MS. POINDEXTER: Right.

DR. KLEIN: And, in addition, the 42-day-old red cell and liquid storage has many changes in the red cell membrane, as you know. It's not at all deformable. It's smaller. It's also lost a lot of red cell membrane, which appears as micro vesicles, which have some thrombogenicity.

So I just want to make sure that we're not holding some of these things to standards that just wouldn't be possible.

MS. POINDEXTER: No, and these are definitely not standards. They're just food for thought.

DR. KLEIN: Ideas. Thank you.

DR. BRECHER: Thank you, Betty.

We're now going to hear from Alan Williams on testing standards and donor eligibility.

MR. WILLIAMS: Thank you.

My charge is to talk about FDA regulatory concerns with respect to donor eligibility and testing. There's been extensive discussion of this already today, so I'm going to move quickly and treat this not only as a recap, but potentially as a posthumous recap. But there are a couple of thoughts that I would like to bring forward.

The first is donor qualification or donor suitability. Everyone thinks in terms of the question administer to the donor on the day of donation, but in fact it's a more extensive process than that, and most of the self-exclusion of donors takes place before the donor ever comes to the blood center. So I think we need to keep in mind that this is a process.

From the very start, exclusion of certain risk populations that may have higher incidents and

prevalence of transfusion-transmitted diseases, self-deferral prior to collection based on collection that the potential donor has available.

There can be self-deferral at the collection site before the interview is actually administered, deferral by staff during the interview, which is the most common factor considered, but in fact tends to be a very low prevalence happening for many of the deferrals, like HIV risk factors. It's really quite rare in the blood center.

And then plus donation information, which the donor doesn't actually bring forward the information at the time of donation, but reports it later.

So I just wanted you to keep in mind the various aspects of donor suitability determination above and beyond the actual question.

This is a slide borrowed from Joy Friday of the AABB Uniform Donor History Task Force Group, and this shows up through 2000 the development of new donor screening questions or subjects that are

turned into questions.

The top line is what has resulted from industry standards--the bottom line, what has been brought forward by the regulators, by memos or guidance documents.

As you can see, there's been rapid growth of new questioning, and I didn't extend this time line, but just simply made a list of some of the potential additions to the donor interview that would impact long-term repository storage.

The one that's received a lot of attention today is the revised travel deferral related to BSE, dietary exposure, potential exposure to variant CJD introduced in January of 2002, recommendations related to recipients of smallpox vaccination in February of 2003.

There have been some new industry standards related to potentially teratogenic medications that have been added to the donor history, and hopefully, in the very near future, we'll be looking at a totally revised uniform donor history questionnaire, which again will set a time

line for a major change in the donor screening process.

I deliberately didn't include in this list some of the other guidance documents that have been released recently, such as the one on donors potentially exposed to anthrax, SARS and West Nile. The reason I didn't include these is because some of these are potentially temporary or emerging infections, and I think, when considering eligibility in a long-term repository, one is more concerned with things that you know are going to be static over time.

Potentially, some of these might be time-limited, and the donor suitability requirements could change as an emerging infection perhaps is no longer part of the blood safety picture at some future time. And I think there's potential for each of these agents to have future consideration as to whether they are long-term threats.

As brought out adequately today, products stored for "extended periods," may not meet current donor's eligibility standards. And an extended

period--it may be years--but, in fact, in the environment we've had over the past year or year-and-a-half, that period could even be measured in months due to the implementation of new questions, and this obviously a hurdle.

In terms of testing, again, a long list of tests that have been introduced over time--not only the tests themselves for individual agents, but new generations and new versions of tests. When a next-generation test for an antibody to a certain marker comes out, again, that sets a new standard for sensitivity of testing for that agent, and then of course the NAT testing for West Nile currently being done under IND.

Instead of showing the time line of addition of new tests, what I showed here is the actual reduction in viral infection from transfusion for HCV, HPV, and HIV. You can see, in the bottom line for HIV, actually, probably the quantitatively largest reduction in post-transfusion risk was due to the donor screening criteria, and then, subsequent to that,

improvements in testing and narrowing of the window period.

And then, similarly, for HCV and HPV, improvements in testing over time have created as much as a thousandfold decrease in post-transfusion risk from these agents. So these changes are, for the most part, a good thing, and I think overall increased the safety of the blood supply.

So, if one is designing a repository or considering an extant repository, what considerations should be made to try to meet future donor eligibility standards and testing standards?

First and foremost, I think periodic rotation of the inventory, which has been mentioned. The time chosen to do that, you know, is something that needs to be given careful thought. Three years, while certainly reasonable in terms of maintenance and turnover of an inventory, it would not keep it current in terms of some of the eligibility recommendations that have just emerged in the past year.

One needs to carefully track the

regulatory status of the products. And I think a most important message here is discuss this assessment with the FDA, in terms of the risk-benefit approach and ways that this might be managed.

There's a variance procedure. Variance is generally related to a variance from a regulation or a guidance document that specifically references a recommendation--a regulation. There can be a supplement to a license application.

This, importantly, does set a precedence. You're actually changing the license, and this then establishes precedent that could be done anywhere by any other license-holder for a similar product.

There are emergency use provisions, combined with medical discretion. There are regs allowing for that. And any of these could be combined with special labeling, as appropriate, for the individual circumstance.

So these are all ways that this can be handled from a regulatory approach, and the best thing to do is just simply discuss the issue with

the Agency and try to find a pathway.

For testing, many testing issues can probably be solved by sample retention. Validation of that sample for the test of interest is a concern. I would offer that NHLBI establishes new repositories approximately every five years, and does a lot of basic research into the type of treatment for this repository that will produce testable sample in the end. And as mentioned, some of the recent REDS repositories and RADAR have actually worked with frozen whole blood, which is easily treated, put into a freezer and allows you to test not only for the plasma RNA but whole blood related nucleic acids that might be there as well. I think this is some good basic work which can help validate samples that are put down.

Related to samples that was touched on today, there are issues of informed consent, and if there's an entirely new assay like a CJD assay, is there an ethical issue regarding whether or not consent was implied in the donation consent and whether or not this needs to be re-accessed.

There needs to be appropriate record retention, including a timeline of procedures in place at the time of collection. The records need to be comparable with the procedures in place so that one can know exactly under what conditions that product was collected.

I included as number 5, although it hasn't been popular in today's discussions, try to maximize the future accessibility to repository donors. It goes a long way if you have subsequent donations from that donor from which information is gained, or if one can access the donor and get what information is feasible to collect to preserve a repository donation.

I'm going to switch gears a little bit at this point and talk about some of the infrastructure issues from a regulatory perspective that were discussed today. Start out with I think a fairly bold statement, that as a necessary component of a strategic reserve and management and deployment of a strategic reserve, there really needs to be ongoing national blood shortage and I

might add inventory monitoring. One really has to know the dynamics of this system, so if one has reserve, one needs to know how large to make it at any given time depending on what the supply situation looks like and where to deploy it to the maximum advantage. I think it could be argued that this needs to be done on a national basis using data from some large blood organizations for available inventory, and I think one can argue that from the transfusion service side, the most usable factor is shortage measurements.

Now, inventory at the transfusions service site certainly has a role because a lot of blood is held there, but if they don't report shortage, then you know there is at least a reasonable inventory, and shortage gives you the way to assess when blood is sufficiently in short supply. That could impact public health and health care.

So what's some of the rationale for making this statement, improve national blood shortage monitoring? The AABB Disaster Task Force has been called together several times, and its role, as you

know, is to coordinate blood needs and blood supply availability, and it utilizes direct communication between the major blood organizations and the blood collectors in areas that are impacted by a particular disaster situation, and this is done in conjunction with federal agency liaisons.

Now, I am one of the liaison members of this group, and I'll say it's a very effective first response measure in times of crisis. It gets everybody together coordinating and works exceedingly well. However, should a situation either be larger scale or multi-site or have a major impact on the donor base, there is no underlying database or predictive capability in existence to support discussions of a coordinating group like this, or indeed for stabilization of the blood supply. As mentioned, this could be related to a large-scale disaster. It could be related to a crisis-induced disruption of the donor base, or as mentioned earlier, something like a widespread donor referral out of a proactive response to something like a smallpox attack.

But I might also add that these data would go a long way toward help smoothing out some of the routine local and regional shortages and allowing us to address some of the, not BT- or CT-related crises, but some of the emerging crises that we've seen. Just knowing the dynamics of the system and being able to bring some predictive data out of what's known as a baseline would go a long way. For instance, in terms of West Nile testing, fortunately we do have a NAT test in place, but in an extremely hot area of West Nile activity, the epidemic tends to be very focused. One would ideally perhaps like to suspend collections for a short period of time in that area. Whether or not you can do that on a large scale would depend on obviously the blood supply. If one had a reserve available, perhaps that way of protecting public health would be more feasible because you knew you had a reserve supply. At some point the line has to be drawn in the balance between supply and protection.

What would be the characteristics of an

improved shortage monitoring network? Sensitivity to local shortage, nationally representative, data available in real time, at a minimum daily, integration of both blood center and transfusion service data, and I think if resources were limited, ideally this would be targeted to inventories at the blood center and shortages at the transfusion service, and it should have predictive capability, sufficiently establish a baseline so that external events can be compared with that baseline and allow prediction in the future, and the data access needs to be broad, not only the private sector collectors and users, but agencies in the HHS and in fact the public.

Now, as most of you know, we've, within FDA, been working on development of a web-based voluntary national reporting system for blood and reagent shortages called TRANS-Net. Because I know most of you have heard this, I'm not going to spend a lot of time on it, but I think I would like to just point out that this system would go a long way toward helping to identify shortages around the

country in real time and use those data to support the deliberations of some coordinating body that could then decide where blood resources might be targeted. The system is designed to be very simple, using data routinely compiled by the facility. It would allow for daily reporting with a reminder by e-mail if the report is not filed. We have devised a standardized definition of blood shortage. Standardized definitions are always a problem, particularly with inventory and shortage, but we have addressed that. And it actually varies a little bit depending on the institution and its capabilities. And we've allowed for a backup reporting option which allows for touchtone telephone entry of data if the Web should happen to be down in a time of crisis.

Being a voluntary system, one major concern is just what's the incentive for participation, and I think this really has to be a grass roots effort with interest in creating data that will help reserve a stable blood supply, making data accessible not only to the collectors

and transfusion services, but to the public at large. Potentially using that also for recruitment efforts would have advantage. Due to the breadth of the program it's not something for which it could be directly, financially supported, at least of the participants.

The system is designed to be population based, encompassing at least first off transfusion services, and hopefully at some level, blood centers, either through the national blood organizations or through individual collectors. Registration in the system is necessary so you have a denominator in terms of who is reporting regularly and who is not. I think it's important to also have a very quick registration available so if a crisis develops, sites that may not have participated previously, may want to enroll, and although that somewhat compromises the denominator, it does allow you to collect quick information in a time of specific need.

Data would be received centrally, and without going into detail, would be managed on an

Oracle database which has been developed and available through GIS mapping, and I think it's important to point out that a lot of these GIS systems do talk to each other, so if blood shortage and availability data were put onto a GIS map, as I'll show you very soon, this could actually be overlaid with some other factors, as were alluded to by the critical infrastructure presenter earlier this morning, that in areas of shortage you could show up to the nearest airport that does in fact have flights available to go in and out. And one can overlay these types of data and make a usable system. And it would be the intent that if appropriate, this could be tied into the larger program.

This very briefly is the registration page for the Web. Simple designation of shortage or no shortage is the first data entry page. If there is a shortage, there are criteria that come up which define that shortage, and I think this is the second major point I'd like to make about this system. Not only does it say where shortage

occurs, but it allows one to define what the potential public health or patient care impact is of that shortage at that particular time. In the current situation, yes, we have blood shortages. At some level they impact patient care, but not to a level of morbidity and mortality. In time of crisis this could change, so some of these factors you may want to measure as to what is the seriousness of a shortage in a given area if blood supplies are not received there very quickly?

I do have a handout which I'll provide. I'm sorry I forgot to do it before the talk, but you can see what the individual criteria are, and they differ for blood centers and transfusion services.

This is a very broad example of a GIS map. You can simply light up with color areas that meet a certain data criteria, and by a click of the mouse you can drill down here, for example, to an individual county level, with levels in this hypothetical example reflecting different levels of blood availability.

This program was piloted early this year. We actually had planned a pilot for January and February of this year. It turns out that that coincides with a somewhat unexpected blood shortage, post-holiday blood shortage, so we actually were able to collect pilot data that matched the time frame of the shortage, and the appeals by Secretary Thompson and the major blood organizations.

Briefly, this is just a graph showing the number of sites reporting shortage in different colors, the transfusions services and the blood centers. One can see that in early January the majority of the pilot participants, of which there were a total of 9, reported shortage. This tended to drop off near the end of February and then there was a slight rebound. I think perhaps what's more interesting is looking at shortage days. Transfusion shortage days during this time frame amounted to 35 percent of the reporting days for blood centers, 48 percent of the reporting days. And we were able to assess a summary of the

characteristics associated with these shortages. They tended to be at the level of use of strategic reserves, delay of medically necessary treatment in one case. Supportive Rh-negative patients with Rh-positive blood happened more than would normally occur, although this sometimes is standard care in some institutions. More than typically would use this form of support did during this shortage period.

In terms of blood centers, all of the pilot sites reporter media appeals, a high proportion use of strategic reserves on 10 days of the pilot period, and a high proportion of the centers reported that they had to cut orders to their transfusion services.

So this program has been developed at least at the initial level, and has been piloted and shown to be feasible within these sites. We are currently in discussions with HHS to try to plan a coordination of this program with the current HHS monitoring program, and get these programs then rolled out so that they are available

both to assess shortages just in a normal ebb and flow of blood availability during the summer and holiday periods, but also to be I think a very relevant response mechanism if the blood supply is challenged.

This program would again go through a second pilot phase to several hundred participants to test the reporting aspects of it, and test the functionality of the mapping function, and then hopefully roll out in full phase to all of the blood centers and transfusion services of the country.

There are potential add-ons for the program, some of which we're doing some developmental work now. One is the ability to report supply and reagent shortages using the same interactive website. We can also potentially collect other data related to that such as we could in fact incorporate inventory measures. We can in fact incorporate platelet supply measures, and it really is modifiable to meet whatever current need exists. We've also built in a function that one

can build in ad hoc questions. If a specific situation exists such a potential anthrax exposure to a blood center, we spend a lot of time within the agency on the telephone to blood centers that may have had collection sites in the anthrax exposure area. This would serve as a conduit of information for that type of message as well.

So I just wanted to reemphasize that I think a program like this would fit well into the infrastructure to support a reserve capacity and deployment of that reserve capacity. And I'll stop here. Thank you very much.

DR. BRECHER: Okay. Time for maybe one question. Chris.

MR. HEALEY: Thanks for the presentation, Alan. The question I had is, is there some standardized data set that's used in the reporting or is the shortage, new shortage relatively subjective? And if it is somewhat subjective, how do you avoid the risk of kind of a creeping permanent shortage?

MR. WILLIAMS: The shortage definition is

based on the criteria. It's expected that if they report a shortage that they will also be able to check one of those shortage criteria so that it can be characterized and reasonably standardized.

Now, the reason we felt that we needed to allow some flexibility, for instance, some transfusion services have frozen repositories, many do not. If one of the sites that has a frozen repository has to tap into it, that is perfectly reasonable to assume that that's a shortage situation, because they wouldn't normally do that. Other institutions might not have the facilities, so they wouldn't report that. So we wanted to build in enough flexibility to keep it relevant for the individual sites. This was assembled in collaboration with an advisory group consisting of blood center and transfusion service directors for the most part, and it seems to have worked during the pilot as we go to a larger scale and may need some adjustment, but that can be done.

DR. BRECHER: Thank you, Alan.

We're going to try to stay on time. We're

going to move on to plasma issues, Julie Birkofer.

MS. BIRKOFER: Dr. Brecher, members of the Committee, thank you very much for the opportunity to be here this afternoon. I'm Julie Birkofer, Director of the Health Policy for the Plasma Protein Therapeutics Association. We wanted to come before you this afternoon to give you an overview of PPTA's efforts to assure a continued, safe, stable and effective supply that assures access and choice for the consumers of plasma protein therapies.

Our data collection effort is coordinated by PPTA and it reflects monthly data, the first day of the month, inventory. This is a voluntary service that our companies provide to the plasma users community. The data is also disseminated to the FDA. It reflects the U.S. market. It is third-party administered. A minimum of three companies must supply data to maintain confidentiality and we have built in verification and audit processes to assure the accuracy of the data.

The type of data that our system reflects is U.S. inventory, emergency supply, distribution, recalls and withdrawals. I know this is a lot of information, and it's small, but just to give you a sense of the definitions that we go by, emergency supply is voluntary, and the companies keep finished products for patients in critical need. Inventory is the first day of the month, and that's where the data is collected, and it includes only product, naturally, that is CBER released as a saleable good. U.S. distribution is the definition, finished product sold from inventory, and it is shipped to the U.S. market within that data month. Recall, absolutely not available for further distribution after a decision is made that the product must be recalled or ceased. And a withdrawal is a internal company decision that the product cannot be distributed.

The utility of the data is that again, aggregated reports are sent to the FDA voluntarily by PPTA monthly. The data is also uploaded on our website in the form of a green, yellow and red

light system. Our light system was launched in September 2002. The status light is based on the ratio of the first day of the month inventory over the average monthly distribution for the previous 12 months. The distribution and inventory ratio data is displayed for a yellow or red light.

Some of the parameters, to give you a sense of when we would go red, is approximately two weeks or less of inventories available. The ratio of inventory to distribution is low and it's less than or equal to .5. A yellow light would be approximately two to five weeks of inventory is available. The ratio of inventory to distribution has declined, and the range is between .5 but less than or equal to 1.25. And again, I would like to point out that these ratios were developed in very close consultation with economists and experts in the field of data collection and analyses. A green light is where we like to be and where we have been for I believe at least over a year. A green light is more than five weeks of inventories available. The ratio of inventory to distribution is adequate

and greater than 1.25.

Emergency supply is a topic that I know you all are interested in today. Again, PPTA member companies reserve a certain quantity of released finished product for patients in critical need. The U.S. distribution data is inclusive of the emergency supply, and the supply that is kept is for IVIG and clotting factors. Yellow or red light, PPTA immediately responds with a communication to the affected stakeholders.

We report our data bimonthly for the affected product categories. We are cooperating with consumer organizations to assure that their needs are being met. For example, the Indeficiency Foundation Supply Safety Net. PPTA hosts minimal quarterly stakeholder meetings to address concerns and any recent supply developments. For example, one of the charts that you would see on our website, this reflects Recombinant Factor VIII from the period September '02, current that we have, June '03, and as you can see, the supply is well, well within the green, and that gives us a lot of

comfort and pride at PPTA and hopefully the stakeholders are equally comforted by that.

That's it. Thank you.

DR. BRECHER: Thank you, Julie.

Questions or comments?

[No response.]

DR. BRECHER: If not, I think we can adjourn early. Take it while you can.

[Laughter.]

DR. BRECHER: We'll meet again tomorrow morning, and start promptly at 8:55. Thank you.

[Whereupon, at 4:55 p.m., the meeting was recessed, to reconvene at 8:30 a.m. on August 22, 2003.]